
Lars Nordström

On Automatic Ventilation

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ON AUTOMATIC VENTILATION

I

A Servo-Controlled Ventilator Measuring
Expired Minute Volume, Airway Flow and Pressure

S. INGELSTEDT, B. JONSON, L. NORDSTRÖM
AND S.-G. OLSSON

II

Haemodynamic Effects of Intermittent
Positive-Pressure Ventilation
With and Without an End-Inspiratory Pause

L. NORDSTRÖM



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INTRODUCTION

Automatic ventilation was first described by WOILLEZ (1876), who constructed an iron cylinder enclosing the body of the patient, with a tight membrane round the neck, and the head of the patient outside the chamber. When pressure in the cylinder was increased the thorax of the patient was compressed, and the lung volume reduced. When pressure in the cylinder was decreased air was again drawn into the lungs.

The apparatus was later developed (DRINKER & SHAW 1929) and used clinically, mostly in treating respiratory insufficiency caused by paralysis.

A simplified variety of this principle was cuirasse ventilation, with a hub covering only the thorax and abdomen of the patient (SAHLIN 1931).

Another type of ventilator, called barospirometer was constructed by the professor of Physiology at the University of Lund, TORSTEN THUNBERG (1924), and tested by ENGHOF (1927).

The whole patient was enclosed in a chamber with changing pressure. When pressure in the chamber was increased, and the pulmonary volume was kept constant, air was moved into the lungs. When pressure was decreased air moved out of the lungs.

Thunberg predicted the use of ventilators in clinical work, the possibility of saving patients with respiratory insufficiency, and the use of curare on patients with tetanus and realized that ventilator treatment would give increased knowledge of the role of respiratory insufficiency in different diseases.

The results with the barospirometer during the first five years were reported by SAHLIN (1932). During this period 10 patients were ventilated, mostly because of central respiratory depression after infection or intoxication. One patient with poliomyelitis was saved by the treatment but died 1½ years later.

Another patient, intoxicated by barbiturate and morphin survived without sequelae.

Modern ventilator treatment uses the principle of intermittent insufflation of gas into the trachea via an endotracheal tube or a tracheostomy cannula, intermittent positive-pressure ventilation (IPPV). Many types of apparatus performing IPPV have been developed since its introduction at the beginning of the 20th century. Several Swedish machines have been constructed (ANDERSSON et al. 1939, ENGSTRÖM 1953, HELLSTEN 1953, HAGLUND & WALDINGER 1955).

One hundred and fifty ventilators, commercially available, are listed by MUSHIN et al. (1969). Besides these, several ventilators have been constructed for experimental purposes. In spite of the great number of ventilator types, it is evident to everyone working in respiratory care, that an improvement of the technical equipment is needed.

A team was formed at the University Hospital of Lund, with the aim of constructing a ventilator according to the resources of modern technique.

One of the main problems was whether a fixed inspiratory pattern was suitable or if inspiration should be variable. At that time (1967) few direct comparisons on ventilatory and circulatory effects of ventilatory pattern were published. With a prototype of the new ventilator some dog experiments were done this year, and some of the results are reported in the report on the haemodynamic effects of IPPV, with and without an end-inspiratory pause (Part II).

The final design of the new ventilator was determined with regard to information from literature, results of the experimental work and an evaluation of the demands that could be expected within the future (Part I).

The ventilator was tested experimentally, and then introduced into clinical usage.

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PART I

A Servo-Controlled Ventilator Measuring Expired Minute Volume, Airway Flow and Pressure

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SYMBOLS AND ABBREVIATIONS

cpm	= Cycles per minute	P_aCO_2	= Arterial carbon dioxide tension, mm Hg
Crs	= Compliance of respiratory system, 1/cm H ₂ O	P_aO_2	= Arterial oxygen tension, mm Hg
EIP	= End-inspiratory pause, % of respiratory cycle	P_{EE}	= End-expiratory pressure, cm H ₂ O
Exp	= Expiration	Pres(rs)	= Pressure overcoming resistance in the respiratory system, cm H ₂ O
f	= Respiratory frequency, cycles per minute	Pst(rs)	= Static elastic recoil pressure of respiratory system, cm H ₂ O
F_{IO_2}	= Fraction of oxygen in inspired gas	Rrs	= Resistance of respiratory system, cm H ₂ O/(1/sec.)
Insp	= Inspiration	V_T	= Tidal volume, l.
IPNPV	= Intermittent positive-negative-pressure ventilation	$\dot{V}$	= Instantaneous flow rate, 1/sec.
IPPPV	= Intermittent positive-positive-pressure ventilation	$\dot{V}_I$	= Minute ventilation, 1/min., numerically equal to inspired minute volume.
IPPV	= Intermittent positive-pressure ventilation		

INTRODUCTION

"Intermittent positive pressure ventilation", IPPV, is being utilized to an ever increasing degree and for an increasing number of indications. Our goal was to construct a ventilator that could satisfy all reasonable technical and medical requirements in all situations. Full selectivity and control of ventilator performance was obtained by means of a new electronic servo-system that provides a continuous control of the airflow to and from the patient.

Information concerning suitable ventilator performance in various clinical conditions is at present limited. Requirements vary with the patient's physiological status: patients with obstructive or restrictive pulmonary disease and with circulatory disturbances may have different optimal insufflation patterns. The ventilatory patterns that are favourable to circulation are as a rule unfavourable to the efficiency of ventilation. The venous return is hampered by high mean intrapleural pressures (COURNAND et al. 1948, MORGAN et al. 1966). Accelerating inspiratory flow, absence of end-inspiratory pause (EIP) and a long expiration would be favourable for the circulation, as may the use of a negative expiratory phase (MALONEY et al. 1953). On the other hand, a negative phase may be hazardous to ventilation especially when used during prolonged periods of time (NUNN 1965 a). It can also be shown theoretically that lung compartments behind obstructed bronchi are best ventilated if inspiratory flow is decelerating, of long duration and followed by an EIP (LYAGER 1968, JANSSON & JONSON 1972). Some of the ventilatory and circulatory effects of an EIP are described by KNELSON et al. (1970), LYAGER (1970) and NORDSTRÖM (1972).

It has been suggested that an even distribution of inspired gas relative to perfusion is

favoured by high alveolar mean pressures (BERGMAN 1963). A similar effect is also achievable with positive pressure during the expiratory phase, i.e. intermittent positive-positive pressure ventilation (IPPPV). It is probable that the better distribution of pulmonary blood flow, and the prevention of alveolar effusions and alveolar and airway collapse, contribute to the effect (CHENEY et al. 1967, 1971, ASHBAUGH et al. 1969, UZAWA & ASHBAUGH 1969).

In normal adults deep breaths occur about 10 times per hour (BENDIXEN et al. 1964 a). This is thought to counteract airway and alveolar collapse. Intermittent hyperinflation is therefore suggested in automatic ventilation as a remedy to reduce the occurrence of atelectasis (FERRIS & POLLARD 1960, BENDIXEN et al. 1964 b).

The clinical importance of different flow patterns under normal and abnormal conditions (WATSON 1962, ADAMS et al. 1970, NUNN 1970) and of periodic hyperinflation (NUNN et al. 1965 b, LUMLEY et al. 1969, BERGMAN 1970, STONE & SULLIVAN 1970) is still debated.

It is well known that patients with chronic airway obstruction have a forced vital capacity which is lower than the vital capacity achieved during a slow expiration. During expiration high flow rates give rise to pressures which may cause dynamic compression and collapse of intrathoracic airways (FRY 1958). High initial flow rates during expiration seem to give low maximum flow rates during the later part of expiration, even in normals (BOUHUYS & JONSON 1967). An expiratory flow regulating device preventing high initial flow rates, but offering no resistance when flow falls late in expiration, would thus have theoretical advantages compared to a constant resistance retarding the expiratory flow.

In order to meet various demands, and to

make possible further research on the optimal ventilatory flow patterns in different groups of patients, it was decided to construct a ventilator that could produce a great variety of ventilatory flow patterns.

Modern intensive care has made clear the importance of continuous control of vital functions by automatic equipment. A modern ventilator therefore ought to include monitoring of pressure and flow, combined with automatic alarms to indicate events which may threaten the efficiency of ventilation.

The danger of cross-infection caused by ventilators is stressed by several authors (PHILLIPS & SPENCER 1965, HELLEWELL et al. 1967, PYLE et al. 1969, CARTWRIGHT & HARGRAVE 1970). The logical solution to this

problem is a ventilator, whose contaminated parts stand routine decontamination and sterilisation.

The technical and medical demands of today, in part discussed above, and consideration of the foreseeable future development in respiratory care, led to the design of the new ventilator.

TECHNICAL DESCRIPTION

The ventilator (Servo Ventilator 900, Elema-Schönander AB, Solna, Sweden) functions as follows: Gases are fed to a bellows, which mixes and stores the gases at a constant pressure that can be regulated between 10 and 100 cm H₂O. From the

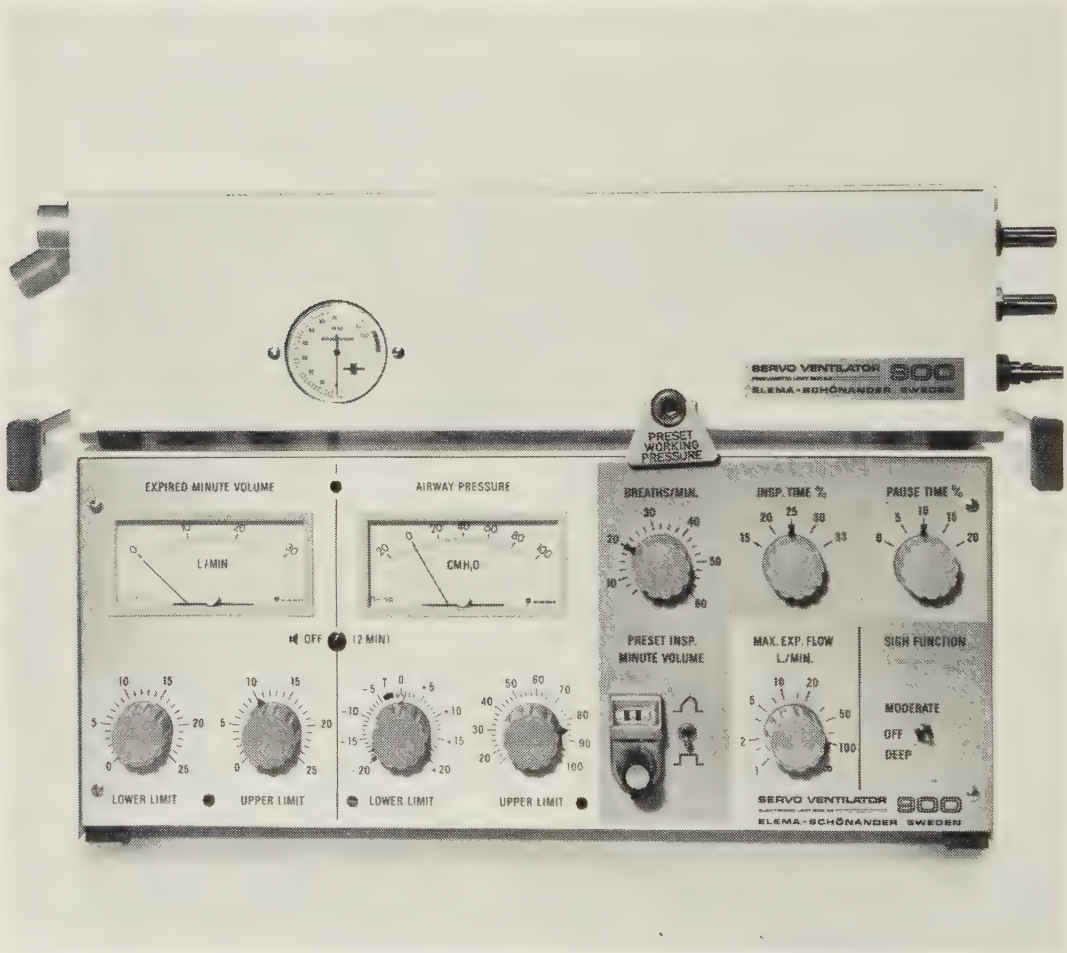


Fig. 1.—The SERVO VENTILATOR.

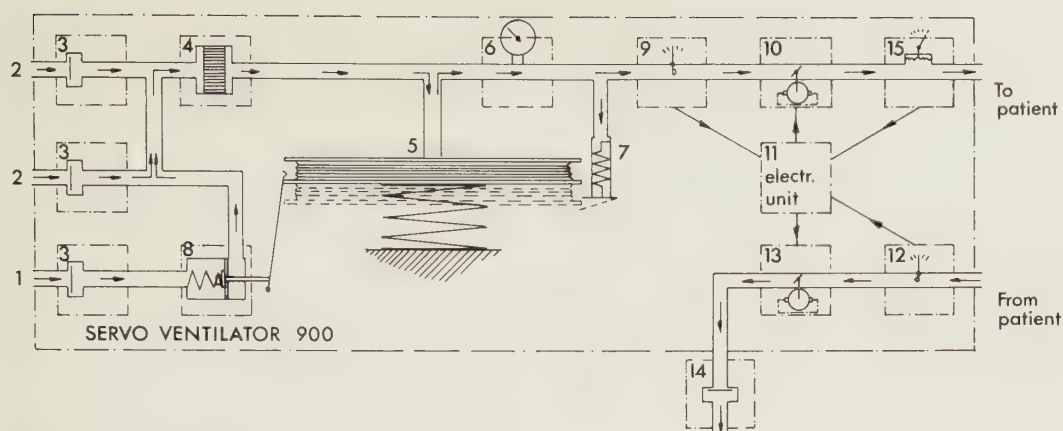


Fig. 2.—Working principles of the ventilator.

1. Air intake from a high pressure source
2. Gas intake from flow regulating devices
3. One way valve
4. Gas filter
5. Springloaded bellows
6. Manometer measuring pressure in the bellows
7. Excess and safety valve
8. "On demand" valve

9. Inspiratory flow-meter
10. Inspiratory choke valve
11. Electronic unit
12. Expiratory flow-meter
13. Expiratory choke valve
14. One way valve
15. Electronic pressure meter, measuring airway pressure

bellows the gas is supplied to the patient via a servo-controlled flow regulator, which regulates the inspiratory flow and volume. A corresponding servo-system controls expiration.

The ventilator consists of a pneumatic unit and an electronic unit (Fig. 1). Their combined dimensions are: height — 30 cm; depth — 23 cm; width — 50 cm. The weight is 10.2 kg for the electronic and 8.1 kg for the pneumatic unit.

The pneumatic unit is connected to the electronic one via a cable but is otherwise detachable and may be placed close to the patient, with the electronic part positioned separately.

The Pneumatic Unit (Fig. 2)

Intake for gas from some kind of high pressure source, 1, or from a flow-meter stand, 2, leads via non-return valves, 3, and a replaceable bacteria proof filter, 4, to a spring-loaded bellows, 5. The internal pressure in the bellows, i.e. the working pressure, is set by means of a special device Pre-Set Working Pressure, Fig. 1).

If a surplus of gas enters the bellows from

the flow-meters, it is released through a safety valve, 7, which opens when the bellows is full.

From the high pressure source the bellows is filled via an "on demand" mechanism, 8, that automatically keeps the bellows half-filled. The bellows thus functions as both a reservoir and a reducing valve down to the preset working pressure. The reservoir reduces the requirements for high momentary inflows of inspired gas from the pressure source. This construction permits the mixing of gases in selected amounts. For example, when mixing air and oxygen the bellows is continuously supplied with the desired flow of oxygen from the flow-meter. During inspiration, when the bellows tends to empty, the "on demand" mechanism will supply the requisite volume of air from the high pressure source, 1, so that the total tidal volume, determined by the preset minute volume and frequency, is obtained.

From the bellows the inspired gas goes to the patient via a flow-meter, 9, and a choke valve, 10. The flow meter controls the choke valve via an electronic circuit in the electronic unit, 11. The servo-system, which has an extremely rapid action, controls the inspiratory

process so that both the preset tidal volume and the desired flow pattern are obtained.

The expired gas leaves the patient via a similar servo-system with a flow meter, 12, a choke valve, 13, and a non-rebreathing valve, 14. The airway pressure is measured by an electronic pressure meter, 15.

All the gas-bearing components can be dismantled and reassembled in a few minutes without tools. They are autoclavable or disposable. Exceptions are the mechanical and the electronic pressure meters, which are protected from contamination by bacteria-proof disposable filters.

As a test of the resistance of material against autoclaving, sterilization of the expiratory parts was done after use on each patient, and of the inspiratory parts, at intervals of about 1 month. Bacteriological control by swab sampling from the inspiratory and expiratory systems was done at regular intervals. In 30 controls no bacterial growth was seen, indicating that no contamination of the inspiratory system occurs and that the sterilization of the expiratory parts was effective.

The Electronic Unit

The electronic unit is a small calculator. Fed with signals from the pressure and flow

meters the calculator controls that the choke valves produce the desired respiratory pattern. If this is impossible within preset pressure limits an alarm signal is given.

The desired respiratory pattern is set on the panel. The possible adjustments of the ventilator are described below. The terms in capital letters refer to the setting devices, Fig. 1.

Inspired minute volume (Pre-Set Insp. Minute Volume). Range 0.5–30 l/min.

Frequency (Breaths/Min.). Range 6 to 60 breaths per min.

Inspiratory flow pattern (Fig. 3). Either square or accelerating, indicated by symbols on the panel. Decelerating flow can be obtained by pressure-generated inspiration. (See below).

Duration of inspiration (Insp. Time %). Range 15–33 % of the respiratory cycle.

End-inspiratory pause (Pause Time %). Range 0–20 % of the respiratory cycle.

Sighs. Hyperinflations occurring once per 100 breaths can be produced. They may be either double (Moderate) or treble (Deep) the tidal volume.

Maximal momentary expiratory flow (Max. Exp. Flow). Range 1–100 l/min.

The pressure in the patient tubing (Air-

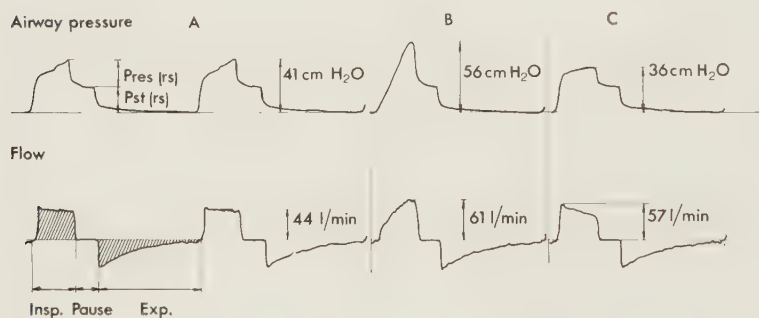


Fig. 3.—Registration of airway pressure and flow from a patient with moderately increased Rrs and decreased Crs.

$\dot{V}_I$ 11 l/min., Insp. Time 25 %, EIP 15 %, f 20 cpm.

A. Constant flow inspiration.

B. Accelerating flow inspiration.

C. Decelerating flow inspiration.

Pres(rs) = 21 cm H₂O. Pst(rs) = 20 cm H₂O.

$$Rrs = \frac{21 \times 25 \times 0.6}{11} = 28.5 \text{ cm H}_2\text{O}/(\text{l/sec}) \text{ (See Eq. 4).}$$

$$\text{Tidal volume} = \frac{11}{20} = 0.55 \text{ l.}$$

$$Crs = \frac{0.55}{20} = 0.028 \text{ l/cm H}_2\text{O} \text{ (See Eq. 1).}$$

Peak airway pressure is highest in B, lowest in C.

The shaded areas graphically represent the volumes of inspiration and expiration.

way Pressure) can be read on the panel. The highest allowable pressure can be set between 15–100 cm H₂O (Upper Limit). If this limit is exceeded, expiration is started and a brief alarm signal elicited. Similarly, if the pressure falls below Lower Limit (range –20 – +20 cm H₂O) an inspiration, giving the preset tidal volume, starts. This is indicated by an optical signal on the panel.

When it is desired to synchronize inspiration with the patient's spontaneous efforts, i.e. patient triggering, the Lower Limit is set for values just below zero.

Lower Limit can be set above zero when IPPPV is desired—e.g., in open chest surgery. At the same time the Max. Exp. Flow should be appropriately limited to prevent a rapid drop in pressure and too early initiation of the next inspiration.

IPPPV can also be achieved by applying a spring loaded valve at the expiration tube. The Lower Limit set at a positive level can then be used to allow patient triggering.

Intermittent positive-negative pressure ventilation (IPNPV) can be obtained by a suction unit applied at the outlet of the expiratory line.

The gas expired by the patient, the Expired Minute Volume, calculated from the expiratory flow, is shown on the panel. It provides a continuous supervision of the patient's minute ventilation. An alarm is given as soon as the ventilation drops below the set Lower Limit, or exceeds the set Upper Limit. The alarm is both optical and acoustical. The acoustical alarm can be switched off for two minutes by means of a push-button (Alarm Off) in case of deliberate interruption of ventilation.

Facilities for Measurements of Pulmonary Mechanics

Electrical signals representing airway pressure, inspiratory and expiratory flow rates, are accessible and can be recorded against time on, for example, an ECG recorder (Fig. 3), or monitored on an oscilloscope. The records obtained allow calculation of the *resistance*, Rrs, cm H₂O/(l/sec), and the *compliance*, Crs, l/cm H₂O, of the *respiratory system*,

which includes the airways, the lungs and the thoracic wall.

Determinations of the elastic properties of the respiratory system must be performed under static conditions, i.e. there must be no pressure gradients due to flow within the system. At the start of an inspiration expiratory flow must therefore have approached zero. At the end of the inspiration an EIP should be used. This must be of adequate duration to allow establishment of a pressure plateau representing the static elastic recoil pressure of the respiratory system, Pst(rs), cm H₂O. In patients with severe airway obstruction the establishment of static conditions before and after an inspiration is not always complete during ordinary breathing patterns. In such patients disconnection from the ventilator for one breath is usually adequate to obtain static conditions before the following inspiration. The use of a long EIP is to be recommended during the measurement for the same reason.

The tidal volume, V_T, l, divided by the pressure established at the end of the pause, Pst(rs), gives Crs. The tidal volume equals the minute ventilation, $\dot{V}_I$, l/min, divided by the frequency, f, cycles per min.

$$Crs = \frac{V_T}{Pst(rs)} = \frac{\dot{V}_I}{f \times Pst(rs)} \quad \text{Eq. 1.}$$

Rrs is defined as the quotient between the pressure overcoming resistance within the respiratory system, Pres(rs), cm H₂O, and the instantaneous flow rate, $\dot{V}_I$, l/sec.

The use of a constant inspiratory flow greatly facilitates the calculation of Rrs. This flow rate, $\dot{V}$, is calculated from $\dot{V}_I$, and the duration of inspiration, Insp. time %, as follows:

$$\dot{V} = \dot{V}_I \times \frac{100}{\text{Insp. time \%}} \times \frac{1}{60} \quad \text{Eq. 2}$$

$$\dot{V} = \frac{\dot{V}_I}{\text{Insp. time \%} \times 0.6} \quad \text{Eq. 3}$$

Pres(rs) can be read from the recordings (Fig. 3), and

$$R_{rs} = \frac{\text{Pres(rs)} \times \text{Insp. time \%} \times 0.6}{\dot{V}_I} \quad \text{Eq. 4}$$

At a moment just prior to the end of an inspiration the pressure recorded is the sum of the pressure which is needed to overcome the elastic recoil pressure of the respiratory system, and the pressure needed to overcome resistance, i. e. Pst(rs) + Pres(rs). In healthy lungs the pressure drops very quickly to Pst(rs) when the inspiratory flow stops. In such cases the separation of Pres(rs) and Pst(rs) is easily and unambiguously done (Fig. 3 and Fig. 6 at Start and at 18 h). In obstructive disease the degree of obstruction generally varies in different lung compartments. The difference in time constants (resistance $\times$ compliance) will result in different speeds at which the lung compartments are filled during inspiration. The most rapid compartments will be overinflated, and will empty their "surplus volume" into the slower compartments during the pause. This "Pendelluft" will show up as a slow establishment of Pst(rs) during the pause (Fig. 6 at 27 hours and 42 hours). In lungs with different time constants there is no unequivocal resistive pressure or resistance (JONSON 1969). We propose, that the resistive pressure is determined in the way shown in Fig. 3. This gives a clinically useful measure of the resistive properties of the respiratory system, provided that the breathing pattern is stated in terms of breathing frequency, the minute ventilation and the insp. time %.

The compressible volume of the ventilator, equipped with rigid tubes to the patient, is very low. If, however, a humidifier with a large volume, or elastic tubes is used, redistribution of air during EIP in form of a flow into the lungs from the ventilator may occur. Such redistribution may cause errors of importance when the magnitude of the compressible volume, compared to the tidal volume, is unfavourable, as it may be in infants. When measuring respiratory mechanics with the ventilator the results have the greatest ac-

curacy, if humidifiers are bypassed and rigid tubes of lowest possible volume are used.

The inspiratory resistance outside the patient, which is included in the resistance measurement, can be measured by detaching the tubing at the tracheal cannula or tube. The airway resistance in the patient is the total resistance measured, minus the resistance outside the patient, measured at the same flow rate.

The inspired tidal volume is represented in the tracings by the area under the inspiratory flow curve, [flow] $\times$ [time] = [volume] (Fig. 3). In the same way the expired tidal volume is equivalent to the area above the expiratory flow curve. The inspiratory flow pattern is not a perfect square wave. It takes up to 0.1 second for the inspiratory flow to rise to its stable value. This inspiratory flow rate must be slightly higher than that theoretically calculated from $\dot{V}_I$ and Insp. time %, in order to compensate for the low flow rate during the first 0.1 second. The difference between the real instantaneous flow rate and that calculated from $\dot{V}_I$ and Insp. time % will cause errors in the determination of R_{rs} according to Eq. 4. These errors are for most practical purposes unimportant. The error is greater when the rise time is a considerable fraction of the duration of inspiration, which is the case at a high frequency and a short Insp. Time %. The correct flow rate can be read from a calibrated flow record from the ventilator and R_{rs} can be accurately determined. This is recommended in scientific applications.

Facilities for Control of Flow and Pressure Meters

If there are no leaks in the tubing system, the inspired and the expired minute volumes should be identical, and the two flow and volume meter systems serve as a control to each other. If a difference should exist, the inspiratory flow can be checked by attaching a calibrator to the inspiratory line. The calibrator is a standard resistance (90 cm H₂O/ (l/sec) at a flow rate of 0.5 l/sec) combined with a mechanical pressure meter. With a preset minute volume of 7.5 liters of air and

an inspiratory time of 25 % the ventilator at a slow frequency and a constant flow pattern delivers a flow of 0.5 liter per second. When the pressure read on the pressure meter is 45 ± 5 cm H₂O the error of the preset minute volume delivered is less than 5 %. The electronic pressure meter can be simultaneously checked by comparison to the mechanical one.

The standard flow rate and pressure, obtained with the calibrator at the settings defined above, gives a convenient means for calibration of a recorder.

The use of a low frequency is necessary since the error caused by the rise time of the inspiratory flow is then negligible.

Calibrations should not be made until a few breaths with the actual setting have passed. The first tidal volumes delivered, after, for example, a change of the resistance to inspiration, are only approximately correct. The error is recognized and memorized by the calculator, which in a few breaths makes the appropriate corrections of the inspiratory pattern to produce the set tidal volume.

The memory function is also used to compensate for occasional low tidal volumes occurring, e. g. when a patient counteracts an inspiration. The following 2–3 tidal volumes will then be larger than preset.

Alternative Working Principles

When the ventilator is used as described above, the ventilation is constant-flow generated and time cycled according to definitions by MAPLESON (1962) and gives the preset minute ventilation regardless of the airway resistance, i. e. volume preset according to definitions by HUNTER (1961).

The ventilator can also perform pressure generated ventilation. The insufflation pressure is then set by regulating the working pressure (Pre-Set Working Pressure). The Pre-Set Insp. Minute Volume is set well above the ventilation desired. The patient's minute volume is then read off from and supervised by the expired minute volume instruments. The minute ventilation can be adjusted to the desired value by altering the working pressure or the respi-

ratory frequency. Pressure generated ventilation results in a decelerating flow, Fig. 3. The possibility of supervising the expired minute volume eliminates the risk of inadequate ventilation, which is otherwise a most important drawback of pressure generated ventilation.

Shift from inspiration to expiration is normally time cycled, but becomes pressure cycled if airway pressure exceeds the set upper limit. Shift from expiration to inspiration is in the same way time cycled, but becomes pressure cycled, when the airway pressure passes the set lower limit.

EXPERIMENTAL RESULTS

The ability of the ventilator to maintain the set minute volume, even with a high and varying airway resistance, was found to be excellent (Table 1). As can be predicted from the working principle of the ventilator, this ability is limited only by the highest insufflation pressure one dares to employ. The use of oxygen and nitrous oxide will cause errors of little practical importance (Table 2).

CLINICAL EXPERIENCE

The clinical experience at the University Hospital in Lund includes more than 600 patients in anaesthesia and 100 patients in postoperative and intensive care, with a treatment time of a total of more than 20,000 hours. The anaesthetized patients were undergoing general surgery, renal transplantation, neurosurgery and thoracic surgery, including open heart operations. In the intensive care patients artificial ventilation was used because of postoperative and post-traumatic pulmonary insufficiency, drowning, tetanus, intoxication, asthma, emphysema, pulmonary oedema caused by cardiac insufficiency, and respiratory distress syndrome.

The smallest child was a premature, weighing 900 grams, with respiratory distress syndrome, who died after 38 hours treatment. The largest patient was a man with postoperative respiratory insufficiency, weighing 195 kg. Ventilation of 2–6 weeks duration was

Table 1.

Test of the ability of the ventilator to produce preset minute volume to a test lung and to measure the expired minute volume correctly. Preset minute volume was compared to the expired minute volume read on the panel meter and measured with a wet gas supply meter (H. WOHLGROTH and Co., Zürich). Working pressure 60 cm H₂O, insp. time 25 %, EIP 10 %, frequency 20 cycles/min. Resistance of the test lung was varied. It was flow dependent and can be described as follows: Resistance A = 7 + 5 $\dot{V}$, Resistance B = 14 + 14 $\dot{V}$, Resistance C = 21.5 + 31 $\dot{V}$ and Resistance D = 80 + 200 $\dot{V}$. Resistance is expressed in cm H₂O/(l/sec) and flow rate, $\dot{V}$, in l/sec. The compliance of the test lung was 0.03 l/cm H₂O at preset minute volume 16–2 l/min., and 0.003 at 1–0.5 l/min. The test lung was a glass bottle filled with aluminium turnings in order to make the compression of gas isothermal.

Preset minute volume l/min.	Measured Minute Volume l/min.							
	Resistance A		Resistance B		Resistance C		Resistance D	
	Panel meter	Wet gas supply meter	Panel meter	Wet gas supply meter	Panel meter	Wet gas supply meter	Panel meter	Wet gas supply meter
16.0	16.0	16.0	16.1*	16.0*	15.0*	15.0*		
8.0	8.0	8.0	7.9	7.9	7.9	7.9	8.0*	8.0*
4.0	4.1	4.1	4.1	4.1	4.1	4.1	4.1	4.1
2.0	1.9	1.9	1.9	1.9	1.9	1.9	2.0	2.0
1.0					1.0	0.9	1.0	0.9
0.5					0.5	0.4	0.5	0.4

* Working pressure 100 cm H₂O.

performed in several patients. The ventilator was found very suitable in all cases, even in the treatment of children and neonates. The

function of the ventilator is not disturbed by use of diathermy equipment.

Table 2.

Test of the ability of the ventilator to produce preset minute volume and to measure the expired minute volume correctly in oxygen and nitrous oxide ventilation. Resistance of the test lung (7 + 5 $\dot{V}$) cm H₂O/(l/sec). Compliance of the test lung was 0.03 l/cm H₂O. Ventilator settings as in Table 1.

Preset minute volume l/min.	Measured Minute Volume l/min.			
	O ₂ ventilation		N ₂ O ventilation	
	Panel meter	Wet gas supply meter	Panel meter	Wet gas supply meter
16.0	16.0	14.8	14.0	14.0
8.0	8.0	7.4	7.5	7.6
4.0	4.1	3.8	4.0	4.1
2.0	2.0	1.8	2.1	2.1
1.0	1.1	1.0	1.0	1.0

Advantages of the Alarm System and the Recording of Respiratory Mechanics

The extensive alarm system and the measuring of respiratory mechanics has been of great importance, giving early recognition of various types of complication, such as airway obstruction and leakage, which can be illustrated by some examples.

Case 1. A 60 year old man with a history of bronchial asthma was submitted for an aortic valve replacement. At the start of anaesthesia he had no symptoms from his asthma. The induction was carried out with dehydrobenzperidol and fentanyl. Succinyl choline was administered prior to the intubation. Muscle relaxation was obtained by diallyl-bis-nor-toxiferin.

The first ten minutes of anaesthesia were uncomplicated (Fig. 4). During preparation

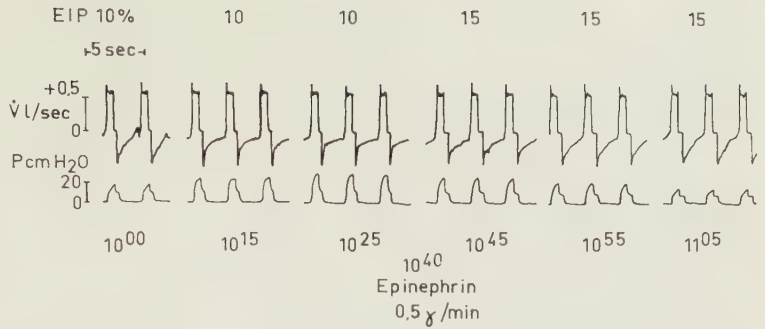
Fig. 4.—*Case 1.* Airway pressure and flow registration from a 60 year old man with a history of bronchial asthma.

Anaesthesia induced at 09.45 a. m.

$\dot{V}_I$ 9 l/min. Insp. time 25 %, EIP 10 or 15 %, f 20 cpm.

Increasing resistance reversed by epinephrine.

Time, a. m.	10.00	10.15	10.25	10.45	10.55	11.05
Rrs, cm H ₂ O/(l/sec)	12	21	29	25	18	12
Crs, l/cm H ₂ O	0.049	—	—	—	—	0.056



for operation 15 minutes later, Rrs began to increase, which was immediately discovered. When Rrs showed a further increase epinephrine was given in a saline drip.

The effect of treatment could be followed. When Rrs decreased the operation was started. It was also noted that the expiratory flow did not fall to zero as long as resistance was high, which means that the patient was in a state of hyperinflation.

Case 2. During the thoracotomy in an infant, 3 months old, a reduction of the expired minute volume was repeatedly indicated by the automatic alarm. From the recorded pressure and flow signals (Fig. 5) it could be seen that the inspiratory flow was unaffected. The expiratory minute volume was continuously lower than the preset minute volume due to leakage between the tracheal tube and the

trachea. In the tracings this shows up as a much smaller area above the V-shaped expiratory flow curve, than under the square inspiratory one (Fig. 5). In the 5th–10th breaths the expired tidal volumes are extremely small. This was due to increased leakage when the mediastinum and trachea were retracted, rather than to air trapping in the lungs, as the peak airway pressure was little affected. Correction of retractor positioning in the operating field could be done under guidance from the flow tracing.

Experience from several cardiac operations on infants tells us that the supervision of ventilation based upon both airway pressure and inspiratory–expiratory flow rates is necessary. It is otherwise not possible to avoid temporary hypoxia, which may elicit ventricular fibrillation in these children with an irritable myocardium.

Fig. 5.—*Case 2.* Airway pressure and flow registration from a thoracotomy on a 3 months old child.

$\dot{V}_I$ 3 l/min. Insp. time 25 %, EIP 10 %, f 25 cpm.

Varying expiratory tidal volumes due to traction on trachea during operation. In breaths No. 5–10 expiratory tidal volumes are extremely low.

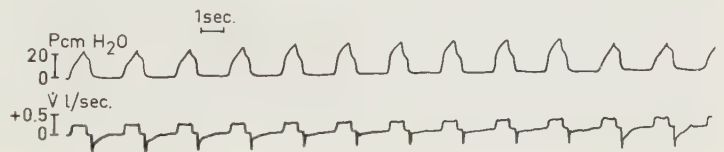


Fig. 6.—Case 3. Airway pressure and flow registration from a 24 year old woman with barbiturate intoxication.

Increasing airway resistance due to secretions obstructing the tracheal tube.

$\dot{V}_I$ 6 and 6.5 l/min. Insufflation time 25 %, EIP 10 %, f 16 cpm.

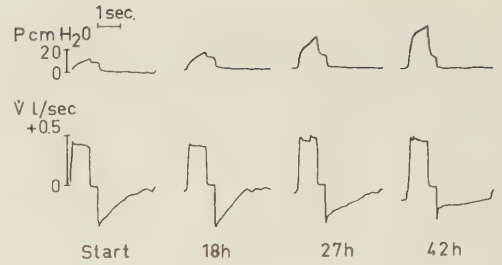
At start, $R_{rs} = 10 \text{ cm H}_2\text{O}/(\text{l/sec})$, $C_{rs} = 0.047 \text{ l/cm H}_2\text{O}$, Time constant 0.47 sec.

After 18 hours, $R_{rs} = 12 \text{ cm H}_2\text{O}/(\text{l/sec})$, $C_{rs} = 0.033 \text{ l/cm H}_2\text{O}$, Time constant 0.40 sec.

After 27 hours, $R_{rs} = 37 \text{ cm H}_2\text{O}/(\text{l/sec})$.

After 42 hours, $R_{rs} = 62 \text{ cm H}_2\text{O}/(\text{l/sec})$.

C_{rs} and time constant were not calculated for the times 27 and 42 hours, as expiratory flow was not zero at the beginning of the following inspiration.



Case 3. A woman with barbiturate intoxication was intubated and ventilated. Recordings of airway pressure and flow rate were obtained with a recorder that automatically registered for 30 seconds every 30 minutes. At the start, Fig. 6, R_{rs} was $10 \text{ H}_2\text{O}/(\text{l/sec})$ and C_{rs} was $0.047 \text{ l/cm H}_2\text{O}$, values which are considered to be normal. Eighteen hours later R_{rs} was slightly increased and C_{rs} relatively more decreased. The expiration was at that time very rapid which was due to the low time constant ($R_{rs} \times C_{rs}$).

After 27 and 42 hours R_{rs} had increased to 37 and $62 \text{ cm H}_2\text{O}/(\text{l/sec})$. Expiration was slow, and the expiratory flow did not approach zero. The patient was in a state of hy-

perinflation. In spite of the high R_{rs} , the ventilator continued to deliver the preset ventilation. The obstruction was found to be due to crusting in the endotracheal tube. The resistance values at 27 and 42 hours correspond to ventilation through tubes with inner diameters of about 5 mm and 4 mm, respectively. This patient was treated at an early stage of the clinical trials with the ventilator. Later on, interpretation of the pressure and flow curves prevented repetition of similar situations. In long-term endotracheal intubation the records give an indication of when it is time for a change of tube or when other measures to reduce airway resistance are needed.

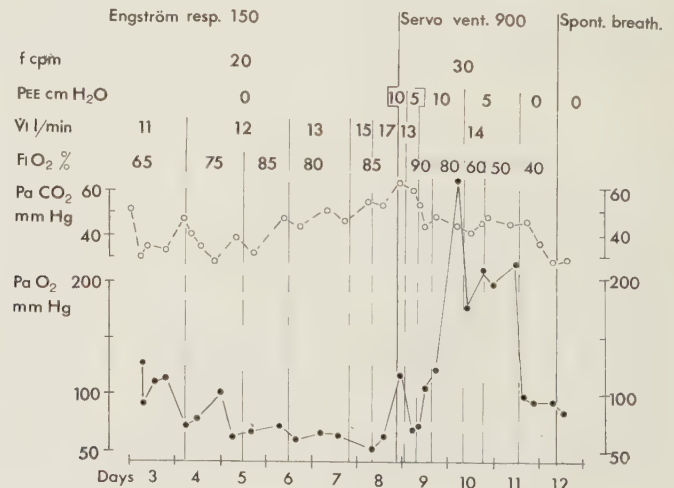


Fig. 7.—Case 4. Effect on Pa O_2 of positive end-expiratory pressure in a 33 year old man with post-traumatic respiratory insufficiency. $F_i\text{O}_2$ = fraction of O_2 in inspired gas.

Application of IPPPV

Case 4. A 33 year old man suffered a rupture of the diaphragm, and fractures of the left femur and mandible in a car accident. His diaphragm was repaired through a thoracotomy. Two days later his clinical state deteriorated, P_aO_2 decreased and he became dyspnoeic. A tracheostomy was performed and he was ventilated with an Engström respirator 150, Fig. 7.

The P_aO_2 slowly decreased in spite of a high oxygen concentration in the inspired gas. After seven days his P_aO_2 was 59 mm Hg and P_aCO_2 51 mm Hg, with $\dot{V}_I$ 14 l of O_2 and 3 l of air per minute. His chest X-ray showed massive bilateral changes in the lung parenchyma (Fig. 8 A). He was in a very poor general condition and was mentally agitated. He had to be heavily sedated and ultimately curarized in order to prevent him fighting against the respirator. At that moment he was put on a Servo Ventilator with a restricted expiratory flow and the Airway Pressure, Lower Limit set at +10 cm H_2O , a level which defines the end-expiratory pressure, P_{EE} . The clinical state improved rapidly. He was calm and curarization was stopped. After one hour the P_aO_2 was 111 mm Hg and P_aCO_2 65 mm Hg. After reduction of P_{EE} to

+5 cm H_2O the P_aO_2 decreased to 65 mm Hg. When P_{EE} was reset at +10 cm H_2O , the same ventilation gave a P_aO_2 of 115 mm Hg and P_aCO_2 of 47 mm Hg. The chest X-ray became almost normal in 2 days, (Fig. 8 B and C). The startling improvement in blood-gases and clinical state allowed a rapid decrease of oxygen admixture and P_{EE} , Fig. 7.

Case 5. A 59 year old man involved in a traffic accident suffered fractures of the left foot, right femur and pelvis, and multiple rib fractures on both sides. Tracheostomy was performed followed by ventilation with an Engström Respirator 150. The P_aO_2 slowly decreased and one week after the accident the P_aCO_2 was about 40 mm Hg and P_aO_2 about 65–70 mm Hg, with 13 l of oxygen and 1 l of air from the ventilator, Fig. 9. He was in a critical state and agitated. No signs of cardiac failure or fluid overloading could be seen, and X-ray of the chest showed no parenchymal infiltration. He was changed over to a Servo Ventilator. A P_{EE} of 8 cm H_2O was achieved by a spring loaded valve at the outlet, which allowed the patient to trigger the ventilator. Within a few hours the P_aO_2 rose to over 100 mm Hg, with P_aCO_2 of the same level as before. His general condition improved remark-

A.

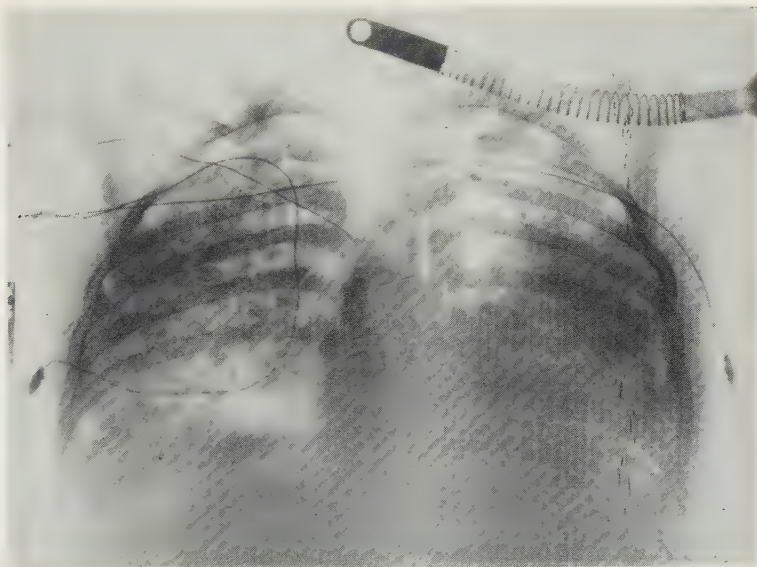


Fig. 8.—Case 4. Effect of positive end-expiratory pressure on chest X-ray picture.

A. Before IPPPV.

B. After 10 hours of IPPPV.

C. After 34 hours of IPPPV.

The parenchymal changes seen in A are reduced in B and have nearly disappeared in C.

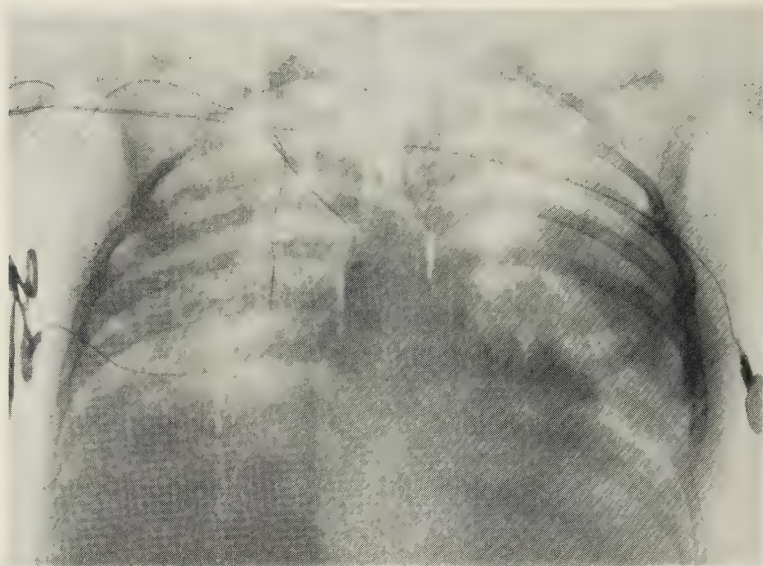


Fig. 8 B.

ably. On return to an Engström Respirator and elimination of the P_{EE} , an increase of the oxygen admixture was needed to obtain adequate oxygenation.

Interference with Circulation by IPPV

Case 6. A 50 year old woman with a severe asthmatic attack shortly after admission to the hospital developed a cardiac arrest.

She was successfully resuscitated and ventilated with a Servo Ventilator. After this episode she had difficulty maintaining her blood pressure at an adequate level. She was digitalized and transfused under control of the central venous pressure, which was continuously about 12 cm H_2O . During the second day the blood pressure fell to 70 and later to 50 mm Hg systolic and she became anuric.

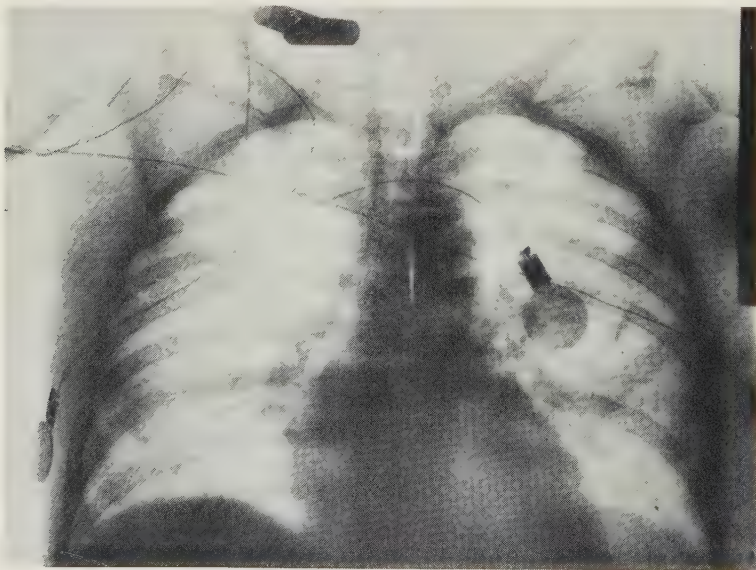


Fig. 8 C.

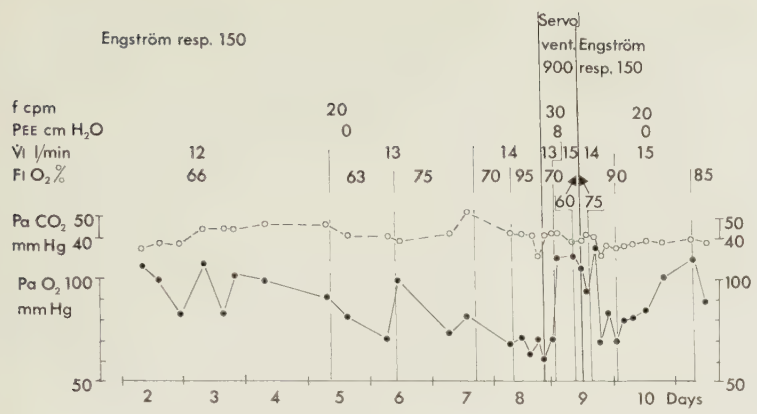


Fig. 9.—Case 5. Effect on P_{aO_2} of positive end-expiratory pressure in a 59 year old man with post-traumatic respiratory insufficiency.

Arterial pH was 7.455, P_{aCO_2} was 35 mm Hg and P_{aO_2} was 117 mm Hg with 50 % of oxygen and a minute ventilation of 11 liters. Insp. time was 20 %, EIP 10 % and the frequency 20 cpm. Rrs was about 45 cm $H_2O/(l/sec)$. In order to substantially decrease the mean intrathoracic pressure and thereby reduce the interference with the circulation the frequency was increased (Nordström, 1972). The arterial pressure was recorded with a pressure transducer connected to a catheter in the femoral artery. An increase of respiratory frequency from 20 to 30 cpm resulted in an increase of systolic blood pressure to 60 mm Hg. When the frequency was further increased to 40 cpm the systolic

blood pressure was 80 mm Hg after 4 minutes and 120 mm Hg after 10 minutes. The central venous pressure did not change. P_{aO_2} was 147 mm Hg, P_{aCO_2} 43 mm Hg and pH 7.420 after one hour at 40 cpm. The arterial pressure stabilized at about 150 mm Hg systolic. The urine production started immediately and was 480 ml during the two following hours. After 4 hours at the breathing frequency of 40 cpm we changed to 20 cpm under continuous recording of the arterial pressure, Fig. 10. In one minute blood pressure decreased from 150/105 mm Hg to 95/70 mm Hg, and in four minutes to 55/45 mm Hg. The frequency was then reset at 40 cpm with immediate response in blood pressure.

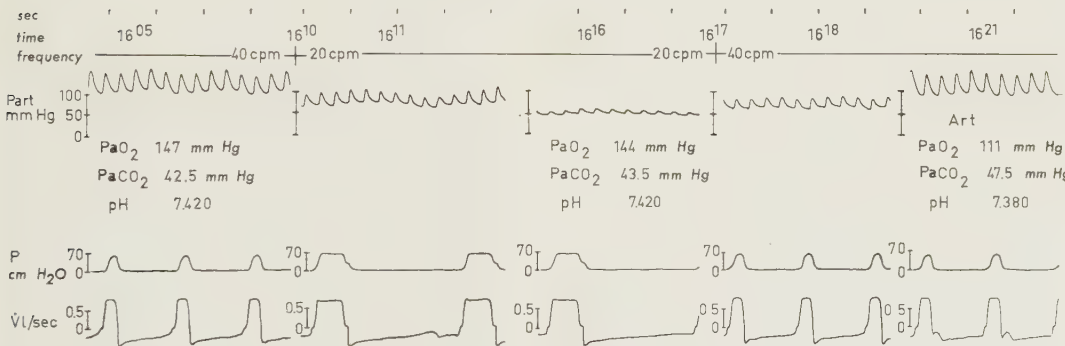


Fig. 10.—Effect on arterial blood pressure of changing the respiratory frequency in a 50 year old woman with bronchial asthma.
 $\dot{V}_I$ 11 l/min., Insp. time 20 %, EIP 5 %.
Rrs approximately 50 cm $H_2O/(l/sec)$ at a flow rate of 0.7 l/sec.

DISCUSSION

The new ventilator described in the present paper offers a unique combination of properties of ventilators, some of which were advised by BENDIXEN et al. (1965) and SAFAR (1965). The great flexibility in the mode of operation was obtained by the application of an advanced electronic technique. This gives not only a nearly unlimited freedom as to the choice of properties of the ventilator, but also eliminates the need for complicated mechanical systems, which may cause problems concerning cleaning, sterilization, and maintenance. It also makes it possible to arrange all setting devices in a logical and easily conceivable way. It is now generally agreed that electronic systems are more reliable in operation than mechanical systems of a corresponding complexity (HILL 1966). The electronic system also allows rapid implementation of features of ventilators that may be wanted in the light of future progress in the field of automatic ventilation.

The ventilator should be regarded as a central unit in a system which may include optional mechanical equipment such as gas mixers, humidifiers, equipment for inhalation therapy, and positive or negative expiratory pressure. The ventilator may also be connected to electronic equipment for monitoring and recording of the pressure and flow signals at a central place in a ward. If computers are accessible in intensive care units, calculations of, for example, compliance and resistance may be automatically performed. It can even be foreseen that the ventilatory performance may be guided by the computer to produce an optimum ventilation.

The problems as to which ventilatory patterns should be used in different types of patients are to a great extent unsolved. Information regarding patients treated in different ways is not difficult to obtain, if patients with little or no pulmonary disease are chosen. In such patients it can be shown that the inspiratory flow pattern has little or no importance as concerns the efficiency of ventilation (WATSON 1962, BERGMAN 1967, ADAMS

et al. 1970). JONSON & NORDSTRÖM (unpublished data) have come to a similar conclusion in experiments on dogs. P_aO_2 , P_aCO_2 , and nitrogen wash out indicated only a minimal increase in the ventilatory efficiency if an EIP of 20 % of the respiratory cycle was added to inspiration. No effect of the flow pattern during inspiration was measurable. This is not surprising. In lungs without severe disease the time constants of different lung compartments are not very different. Each lung compartment will therefore obtain a fair share of the tidal volume during inspiration, irrespective of the flow pattern.

HERZOG (1964) advocates the use of an accelerating inspiratory flow. "Through the acceleration of gas-flowrate and pressure, the stenosed bronchi are expanded, so that even during the period of high gas-flowrate towards the end of the dynamic insufflation the more difficultly accessible alveoli can be inflated without over-extending the open alveoli". A theoretical analysis based upon a digital computer shows the opposite: a *decelerating* flow gives the most even ventilation to lung compartments with different resistance, and the lowest pressure in the open lung compartments (JANSSON & JONSON 1972). Accelerating flow during insufflation is to be recommended mainly in patients with a critical circulatory insufficiency, and then without an EIP.

The EIP may be regarded as a prolongation of the inspiration. The inspiratory flow pattern may be characterized as early lung filling, irrespective of the flow pattern during the insufflation time proper, when an EIP is used. The effect of an added EIP or of a prolongation of the inspiration is a lowered quotient between the physiological dead space and the tidal volume in experiments performed on healthy subjects or dogs (WATSON 1962, BERGMAN 1967, LYAGER 1970). The effect is small, especially if the inspiration time is above 1 second. When inspiration is shorter than 1 second, the gas mixing even in normal lungs must be expected to be affected, resulting in a decreased efficiency of ventilation (HORSFIELD & CUMMING 1968).

In the critically ill patient, e.g. one with

severe status asthmaticus, it is very difficult to get reliable data as concerns the efficiency of different flow patterns. These patients are, of course, in a very unstable condition. Their state changes from one minute to another due to the nature of the disease and to the necessarily intense efforts in treatment.

We have failed even in animal experiments to produce airway obstruction, which was stable enough to allow precise studies of the efficiency of ventilation and its dependency on flow patterns. It is also in most hospitals hardly practicable to obtain series homogeneous and large enough to allow conclusions to be drawn concerning the importance of a single factor such as the inspiratory flow pattern.

It can be shown that the effect on the circulation of the inspiratory flow pattern and the EIP is very small in dogs with intact circulatory system and lungs (LYAGER 1970, NORDSTRÖM 1972). It could, however, be shown that when the function of the circulatory system was depressed, even minor changes in the ventilatory pattern were of importance (NORDSTRÖM 1972). The introduction of an EIP of moderate duration, causing a rise of the mean oesophageal pressure of only 1 cm H₂O, caused considerable circulatory depression. Nordström also showed the importance of the respiratory frequency as a determinator of the mean intrathoracic pressure, which suggests the use of a high respiratory frequency in patients with circulatory failure. This mechanism is dramatically illustrated by case 6 above.

The effect of varied ventilatory rate on circulation is seldom noticed in the literature. It is known that in lung emphysema an intralveolar pressure rise will cause an abnormally high increase in pleural pressure, because of the diminished elastic recoil of the lungs (HEADLY-WHYTE et al. 1966). In treatment of patients with acute asthma most authors recommend ventilatory rates of 20 or slower (WILLIAMS & CROOKE 1968, SYKES et al. 1969). It is however, important to know that a circulatory depression may be reduced by increasing ventilatory rate.

Our conclusion is that a long inspiration,

decelerating flow rate, and an EIP are favourable to ventilatory efficiency and unfavourable to circulation. The theories have in many aspects been verified in experimental studies. We have, from our experience with the ventilator, become convinced that the use of settings which are favourable to the most seriously affected function of a critically ill patient should be used. The margins between deterioration and improvement may in these patients be so small that effects negligible in normal individuals are crucial.

Regulation of the expiratory flow and airway pressure has aroused increasing interest. As mentioned, a high expiratory flow rate may jeopardize the emptying of lung compartments with a high resistance. YOUNG et al. (1963) have shown that a low expiratory flow rate favours emptying of compartments with a low ventilation to perfusion ratio. LICHTNECKERT (1967) showed that expiration through an added resistance results in a more even distribution of ventilation in subjects with histamine-induced bronchoconstriction. In our opinion the likely explanation for this effect is a reduction of the expiratory peak flow rate. We have not found any experimental studies in which a flow regulator has been used to limit the expiratory flow rate during IPPV. We still lack adequate experience on its use for the purpose of promoting the emptying of slow lung compartments and thereby the evenness of ventilation. However, the theoretical foundation and the sparse experimental support would justify the use of the expiratory flow regulator for this purpose, preferably under guidance from expiratory flow tracings. *Max. Exp. Flow* should be so set that the initial expiratory flow peak is cut off, without interference with the later part of the expiration.

In patients with severe asthmatic attacks the problems of distribution of ventilation are most prominent. To promote filling of highly resistive lung compartments a pressure generated inspiration is ideal from the theoretical point of view. The preset airway pressure, in the Servo Ventilator—Preset Working Pressure, is then applied at the entrance of the obstructed bronchi from the beginning

to the end of the inspiration. The airway pressure, which may involve risks if high pressure is used (MACKLIN & MACKLIN 1944, OVENFORS 1964) is in pressure generated ventilation kept within an optimally low limit, but is efficiently used to fill the slow compartments. The limitation of the expiratory flow rate may simultaneously be used to promote emptying of these compartments. It may involve a risk of hyperinflation if the expiratory flow is set at too low a value. This combination of inspiratory and expiratory flow patterns is unfavourable to circulation. The patients must be carefully observed with regard to these risks.

The use of a positive expiratory pressure, IPPPV, has been suggested in several types of disease, such as in pulmonary oedema (BARACH *et al.* 1938), in cases with critically crushed chests (AVERY *et al.* 1956), in patients with severe respiratory failure (ASHBAUGH *et al.* 1969, MCINTYRE *et al.* 1969, KUMAR *et al.* 1970), after heart operations (HILL *et al.* 1965, CHENEY *et al.* 1967, SEED *et al.* 1970) and in idiopathic respiratory distress syndrome in infants (GREGORY *et al.* 1971).

The value of IPPPV is heavily documented in reports confirming the original observations. We have used IPPPV, often with a dramatic effect, such as in cases 4 and 5. The new ventilator offers different ways to produce IPPPV. The use of a spring loaded valve at the outlet has the great advantage that it will still allow patient triggering of the ventilator. This will in most cases eliminate or strongly reduce the problem of the patient breathing out of rhythm with the ventilator, and it will give the patient the possibility of increasing the ventilation on demand. We feel it is most valuable to avoid heavy sedation and curarization, as such measures are liable to reduce autonomic regulation, muscle tone, the venous return and in general the defense mechanisms of the patient, at a time when he needs them most. Our experience is that in most cases the use of IPPPV considerably increases the arterial oxygenation. Elimination of hypoxia has a calming effect and thereby reduces the oxygen consumption. Both factors

reduce the need for sedation of the patient.

In many patients in a moderately severe clinical state, a sufficient effect, in principal similar to that of IPPPV, may be obtained by prolonging the inspiration and the EIP. The expiration is thereby shortened and the mean intra-alveolar pressure increased. A moderate limitation of the expiratory flow rate may be used to give additional effect. Our ventilator thereby gives means for easy, safe and flexible control of the expiration in these patients.

Our positive experience on the value of measurements of compliance and resistance is illustrated by cases 1 to 3.

The measurement of the expired minute volume is the best safeguard against complications such as severe obstruction and leakage. Its value is enhanced by the small volume of compressible gas in the ventilator. Gas compression within the ventilator and tubing will "steal" only a little of the insufflated air, and similarly contribute little to the expired minute ventilation. This is important especially in infants in whom leakage between the uncuffed tube and the trachea is the rule and in whom tidal volumes are small. In infants the observation of expiratory and inspiratory flow patterns are recommended as a complement to the monitoring of expiratory minute ventilation (case 2).

The measurement of the expired minute volume in combination with the flexible mode of operation of the ventilator may be helpful in training patients to breathe spontaneously. Training may be performed as follows. The ventilator is set for pressure generated ventilation. In order to avoid temporary hyperventilation the working pressure is at first reduced to a value close to the peak airway pressure observed at the electrical manometer. The preset inspiratory minute volume is increased to a value well above the desired minute ventilation. The ventilation is now pressure generated and time cycled. The frequency is then reduced to a value below that desired by the patient. The ventilation is now pressure generated and patient cycled. The patient can regulate the minute ventilation by choosing a suitable frequency or by applying an inspiratory muscular effort to increase the

tidal volumes. The working pressure may be successively reduced, simultaneously with encouragement to the patient to produce more and more of the power needed to produce an adequate ventilation. The ventilation can be continuously controlled on the expired minute volume meter. Training periods with less and less support from the ventilator and prolonged periods of time may be undertaken. Such training under the control and support from the ventilator has been found to be effective and comfortable for the patient. In addition it gives information on the progress of the patient as concerns his ability to maintain his ventilation. The need for repeated determinations of arterial blood gases is reduced.

Automatic ventilation of the lungs is a wide medical field, due to the greatly diversified spectrum of patients with manifold clinical problems. Our experience with the new ventilator is, in this light, limited. We have, for example, as yet not studied the effects of intermittent hyperinflation, sighs.

The flexibility of the ventilator makes it very suitable for use in the most critically ill patients. It may be argued that one or other feature of the ventilator is dispensable. Be that as it may, such a feature is nevertheless justified at present in order to make possible research necessary for future simplification.

SUMMARY

A ventilator based upon a new working principle is described. An electronic servo-system, including a flow measuring device and a flow regulator in both the inspiratory and the expiratory lines, provides a continuous control of the gas flow to and from the patient. The ventilator performs flow and volume or pressure generated ventilation with various inspiratory flow patterns. The shifts between the ventilatory phases are basically time cycled, but can also be pressure cycled. The ventilator has facilities for automatic intermittent hyperinflation. Electronic measuring devices continuously supervise minute ventilation and airway pressure. Flow and pressure signals are

provided and allow easy calculations of resistance and compliance. Calibration is obtained by a simple standard resistance. Parts in contact with the respiratory gases can be readily detached and reassembled. They are autoclavable or disposable.

The ventilator was tested in anaesthesia and advanced respiratory care. It introduces possibilities to select a working pattern of the ventilator, suitable for the patient. The importance of a flexible mode of operation to fulfil the varying demands of critically ill patients is illustrated. The continuous control of expired minute volume was considered to be the best safeguard for the patient. The clinical value of determinations of resistance and compliance is shown.

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PART II

Haemodynamic Effects of Intermittent Positive-Pressure Ventilation With and Without an End-Inspiratory Pause

L. NORDSTRÖM

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SYMBOLS AND ABBREVIATIONS

Ventilation

cpm	= Cycles per minute
EIP	= End-inspiratory pause % of respiratory cycle
Exp	= Expiration
Insp	= Inspiration
IPNPV	= Intermittent positive-negative-pressure ventilation
IPPPV	= Intermittent positive-positive-pressure ventilation
IPPV	= Intermittent positive-pressure ventilation
P _a CO ₂	= Arterial carbon dioxide tension, mm Hg
P _a O ₂	= Arterial oxygen tension, mm Hg
P _{alv.}	= Alveolar pressure, cm H ₂ O
P _{ao}	= Pressure at airway opening (or in tubes between ventilator and patient), cm H ₂ O
P _{oe}	= Oesophageal pressure, cm H ₂ O

Circulation

G _{pulm}	= Conductance of pulmonary vascular system (ml/min)/cm H ₂ O
G _{syst}	= Conductance of systemic vascular system (ml/min)/cm H ₂ O
$\bar{P}$	= Mean pressure
P _{art}	= Systemic arterial pressure, mm Hg

P _{l,atr}	= Left atrial pressure, cm H ₂ O
P _{pulm.art}	= Pulmonary arterial pressure, cm H ₂ O
P _{r,atr}	= Right atrial pressure, cm H ₂ O
$\dot{Q}$	= Momentary blood flow, ml per minute
$\bar{Q}$	= Mean blood flow, ml per minute
SV _{lv}	= Stroke volume of the left ventricle, ml
SV _{rv}	= Stroke volume of the right ventricle, ml
SW _{lv}	= Stroke work of the left ventricle, g cm
SW _{rv}	= Stroke work of the right ventricle, g cm

Statistics

n	= Number of observations
M	= Mean value
SD	= Standard deviation
t	= Student's t-value
—	= Non-significant difference, P > 0.05
*	= Probably significant difference, 0.01 < P ≤ 0.05
**	= Significant difference, 0.001 < P ≤ 0.01
***	= Highly significant difference, P ≤ 0.001

During recent years, an end-inspiratory pause (EIP), i.e. a retention in the lungs of the insufflated tidal volume, has been discussed as a means of obtaining an improved gas distribution in the lungs during intermittent positive-pressure ventilation (IPPV). Studies on the immediate effect of EIP on the circulation do not seem to have been performed.

A new ventilator offered a possibility of studying the differences between ventilation with and without EIP.

REVIEW OF THE LITERATURE

The momentary and overall effects of artificial ventilation have been the object of extensive studies in animals and man.

The following may serve as an example:—The momentary flow variations in spontaneous respiration in the dog were described by MORGAN et al. (1966 a) as follows: "The negative intrathoracic pressure of inspiration causes an increased effective filling pressure of the right heart, demonstrated by a forward surge in the venae cavae, superimposed on the cardiac pulsation. This surge is reflected, within a beat or two, by an increase in stroke volume from the right ventricle". The increase in the right ventricular stroke volume led to an increase in the stroke volume from the left ventricle either immediately or at the most within two beats.

Circulatory Pattern in IPPV and Valsalva's Manoeuvre

MORGAN et al. (1966 b) reported that the momentary flow pattern in IPPV is somewhat different from that in spontaneous respiration: "The surge in vena caval blood flow which normally occurs with spontaneous in-

spiration occurred in IPPV during expiration, at a time when intrathoracic pressure was approaching zero".

The vena caval flow decreases during insufflation; the flow in the pulmonary artery follows within one beat, and the aortic flow within two beats. In man, the vena caval flow shows the same pattern (MORGAN et al. 1968). The pulmonary blood volume decreases during the insufflatory phase owing to a smaller outflow from the right as compared with the left ventricle, thus increasing the pulmonary vascular resistance.

The intrathoracic pressure changes in IPPV are normally small, but in pathological conditions they may reach high values. The momentary effect of very large increases in the intrathoracic pressure has been analysed in relation to studies of "Valsalva's manoeuvre", i.e. "a sudden sustained rise of intrathoracic pressure" (SHARPEY-SCHAFER 1963).

At first the increase in the intrathoracic pressure results in an initial rise in the arterial pressure on account of the mechanical influence on the large intrathoracic arteries. Then a fall in the arterial pressure occurs simultaneously with a decrease in cardiac output. After a couple of seconds, the arterial pressure is stabilised, or it may even increase, due to reflex vasoconstriction elicited through receptors in the carotid sinus and the aortic arch.

When the intrathoracic pressure again approaches normal, the arterial pressure shows an initial fall followed by rise occurring simultaneously with an increase in cardiac output. The vasoconstriction persists for a short while, and an "overshoot" in the arterial pressure occurs before it returns to the initial value.

If the vasoconstrictor reflexes are absent, the arterial pressure continues to fall as long as the intrathoracic pressure is increased, and no "overshoot" occurs when the intrathoracic pressure returns to normal.

IPPV can be regarded as a prolonged Val-salva manoeuvre (WATSON et al. 1962).

Effect of IPPV on Cardiac Output, Arterial and Venous Pressures

On changing from spontaneous respiration to IPPV a high intrathoracic mean pressure develops (OPIE et al. 1961). In normal individuals, a compensatory increase occurs in the pressure in the peripheral veins, while the arterial blood pressure and cardiac output are scarcely affected (MALONEY et al. 1953).

With the occurrence of great changes in the intrathoracic mean pressure or in the presence of a diminished compensatory capacity in the venous system, IPPV results in a fall in cardiac output and arterial pressure. Such failures of the compensatory mechanism have been demonstrated in spinal anaesthesia (SARNOFF et al. 1950), ganglionic blocking (PRICE et al. 1954), after large doses of barbiturates (MALONEY et al. 1951, PRICE et al. 1952), in hypovolaemia (BEECHER et al. 1943, MALONEY et al. 1953, VIRTUE et al. 1961) and in poliomyelitis (BERNEUS & CARLSTEN 1955). In IPPV, cardiac output is decreased in patients who have undergone thoracic surgery (GRENVIK 1966). The circulatory effect of various methods of ventilation is believed to be related to the intrathoracic mean pressure (COURNAND et al. 1948, MOTLEY et al. 1948, MALONEY et al. 1953, MALONEY & HANDFORD 1954, PRICE et al. 1954, MORGAN et al. 1966 b, 1967, 1968). Differences in intrathoracic mean pressure may be caused by variations in the inspiratory phase. Theoretically, the greatest flow in the initial phase of the inspiration (decelerating flow, early filling of the lung) results in a somewhat higher intrathoracic mean pressure than if the greatest flow is in the end of the inspiratory phase (accelerating flow, late filling of the lung (ADAMS et al. 1970)). However, the circulatory effect of these flow differences is relatively slight. In experiments on anaesthe-

tized dogs, ADAMS et al. (1970) were thus unable to demonstrate any cardiorespiratory difference between the various flow patterns.

The incorporation of an EIP in the inspiratory phase, will always result in early filling of the lungs, and the inspiratory phase as a whole can be said to assume the character of a decelerating flow, and the initial insufflation pattern becomes less important. LYAGER (1970), in anaesthetized dogs, observed a reduced cardiac output when an EIP was added to the insufflation.

Prolongation of the inspiratory phase in relation to the expiratory phase increases the intrathoracic mean pressure and may lower the cardiac output (BERNEUS & CARLSTEN 1955, MORGAN et al. 1966 b). A prolongation of the inspiratory phase in the form of an EIP gives strictly definable increase in the alveolar pressure without changing the tidal volume and is therefore suitable in studies of the circulatory effects of the intrathoracic pressure.

The expiratory pattern may exert a great influence on the intrathoracic mean pressure. An increased flow resistance increases the pressure level. A positive or negative pressure during the expiratory phase is often used experimentally and in clinical practice in order to influence the intrathoracic pressure. When a negative pressure is applied to the airway during expiration, i. e. intermittent positive-negative-pressure ventilation (IPNPV), the intrathoracic mean pressure is reduced. Comparisons performed at the change from IPPV to IPNPV show no or only an insignificant difference in the circulatory effect in individuals with intact circulatory reflexes (MALONEY et al. 1953, WATSON et al. 1962), in patients under anaesthesia (PRYS-ROBERTS et al. 1967) and in patients who have undergone thoracic surgery (GRENVIK 1966).

In patients with circulatory inadequacy, MALONEY et al. (1953) observed a lower cardiac output in IPPV as compared with IPNPV.

WATSON et al. (1962), in a comparative study of IPPV and IPNPV, in patients with blocked circulatory reflexes found a reduction in the mean transmural central venous pres-

sure, and an inhibition of venous return which was directly related to the increase in the intrathoracic pressure.

Positive pressure during the expiration, intermittent positive-positive-pressure ventilation (IPPPV), often described as continuous positive-pressure ventilation (CPPV), has for a long time been used in open-chest operations and as a method of treatment in cardially conditioned pulmonary oedema (BARACH et al. 1946) as well as in chest traumata (AVERY et al. 1956), and it has recently been employed in other forms of respiratory insufficiency (ASHBOUGH et al. 1969, KUMAR et al. 1970, GREGORY et al. 1971).

In IPPPV, a circulatory inhibition of varying degree occurs. In anaesthetized dogs, SYKES et al. (1970) demonstrated a reduction in cardiac output amounting to about 25 % at an expiratory positive pressure of 10 cm H₂O. In patients with severe pulmonary insufficiency, MCINTYRE et al. (1969) found that a positive pressure of 5 cm H₂O did not affect cardiac output. In relation to the positive-pressure treatment the P_aO₂ improved in these patients.

In addition to its mechanical influence, IPPV may affect the circulation through the changed conditions for the consumption and uptake of oxygen (CLOWES et al. 1965, GRENVIK 1966) and also through changes in P_aO₂, P_aCO₂ or pH (KONTOS et al. 1965, SUUTARINEN 1966, PRYS-ROBERTS et al. 1967, MORGAN et al. 1967, 1969).

Pulmonary Vascular Resistance

The pulmonary vascular resistance is changed when gas is insufflated into the lungs. This problem has been studied by WHITTENBERGER et al. (1960), ROOS et al. (1961) and others. The mechanism of action is fairly complex. "The unusual distensibility of the small pulmonary vessels, i. e., of the pulmonary "resistance" vessels affects their hemodynamic behavior. For example, as the pulmonary blood volume is expanded, small pulmonary vessels share in this increase, leading to an increase in their transmural pressure, passive dilatation of their lumens and a

decrease in their resistance to blood flow" (FISHMAN 1963).

The transmural pressure in the pulmonary blood vessels is determined by the pressure of the contents of the vessels in relation to the surrounding pressure. The internal (intraluminal) pressure depends on the output of the right ventricle, the resistance in the pulmonary circulation, the pressure in the left atrium and the hydrostatic conditions. The external (extramural) pressure is determined by the pleural and intrapulmonary pressures.

The extramural pressure in the lungs varies with the height of the pulmonary tissue. This variation is of the order of 0.25 cm H₂O per cm lung distance (GLAZIER 1966). The extramural pressure of the extrapulmonary vessels is also influenced by the body position (BROOKHART 1947, WIGGERS 1947).

Thus, the transmural pressure of the pulmonary vessels differs in the various regions of the lung. PERMUTT et al. (1962) suggested a division of the lung into three zones, which were described as follows by WEST (1965) (Fig. 1): "In zone 1 arterial pressure is less than alveolar pressure, and there is no flow, presumably because collapsible vessels are directly exposed to alveolar pressure. In zone 2 arterial pressure exceeds alveolar, but alveolar pressure exceeds venous. Here the vessels behave as Starling resistors, that is, collapsible tubes surrounded by a pressure chamber; and flow is determined by arterial pressure minus alveolar, not arterial minus venous. In zone 3 venous pressure now exceeds alveolar, the collapsible tube is held open, and flow is determined by the arterial-venous pressure difference".

The extrapulmonary vessels also play a certain part, and a zone 4 was suggested by HUGHES et al. (1968). The factors considered here are the effect of the interstitial pressure and the mechanical effects of traction and compression on the extrapulmonary vessels.

The effect of the insufflation on the pulmonary vascular resistance was measured in the closed chest by SIMMONS et al. (1961) and others. They found the lowest vascular resistance at a lung volume corresponding to the functional residual capacity. The resist-

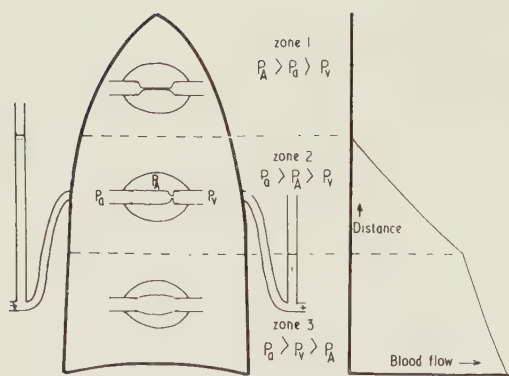


Fig. 1.—Relations between pulmonary blood flow and alveolar pressure (P_A), pulmonary arterial pressure (P_a) and pulmonary venous pressure (P_v). (After West 1965). See text.

ance increased steeply with increasing pressure and lung volume, but it also increased with decreasing pressure and lung volume to a lesser extent.

The pulmonary vascular resistance is also affected by chemical factors, such as PO_2 , PCO_2 and pH (DUKE 1957, SHAPIRO et al. 1966, VILES & SHEPHERD 1968, ARBORELIUS 1969).

Venous Return—Right Atrial Filling Pressure

“The term ‘venous return’ means very simply the flow of blood from the veins into the heart. Though venous return is normally exactly equal to ventricular output, this may not be true for short periods of time. However, when the venous return is greater than the ventricular output, blood will accumulate in the heart. During the ensuing few heartbeats a new state of equilibrium will develop, and venous return will again become equal to the output” (GUYTON 1963).

Thus, in the study of the momentary effect of the ventilation on the blood flow ‘venous return’ is not a suitable parameter. A more adequate object of study seems to be the force with which the venous blood fills the heart. WERKÖ (1947) measured the net filling pressure of the right ventricle (transmural pressure) and demonstrated that this was reduced in IPPV as compared with spontaneous respi-

ration. He emphasized the normal correlation between net filling pressure and stroke volume. Similar analyses were performed by Cournand et al. (1948).

The transmural central venous pressure in IPPV was studied by WATSON et al. (1962), who demonstrated a correlation between a reduced transmural venous pressure and low arterial blood pressure.

Right Atrial Filling Pressure—Stroke Work of Right Ventricle

SARNOFF & BERGLUND (1954) showed that the stroke work of the right ventricle is correlated to its filling pressure as “Starling’s law of the heart states that the energy of contraction, however measured, is a function of the length of the muscle fibers prior to contraction”.

According to SARNOFF (1955), the atrial pressure can be used as a measure of the ventricular filling pressure: “The correlation between mean atrial pressure and end-diastolic ventricular pressure was satisfactorily close in the low and medium ranges”.

The stroke work of the right ventricle is usually expressed by the formula: —

$$SW_{rv} = SV_{rv} (\bar{P}_{p_{\text{pulm. art}}} - \bar{P}_{r. \text{atr}}).$$

In this formula, the small amount of energy required for the acceleration of the blood and the immeasurable energy losses in the heart muscle are disregarded (RUSHMER 1961).

In the dog, a linear relationship often exists between the right atrial filling pressure and stroke work (SARNOFF & BERGLUND 1954; Fig. 2).

The relation of the stroke work to the filling pressure may be affected by changes in the contractility of the heart muscle provoked by shifts in the physiological and chemical environment, and by great changes in the heart rate (SARNOFF 1955).

Within short periods of time, in the presence of a regular heart rhythm, changes in the stroke work will reflect variations in the filling pressure.

At the same time, the stroke work of the right ventricle constitutes a measure of the

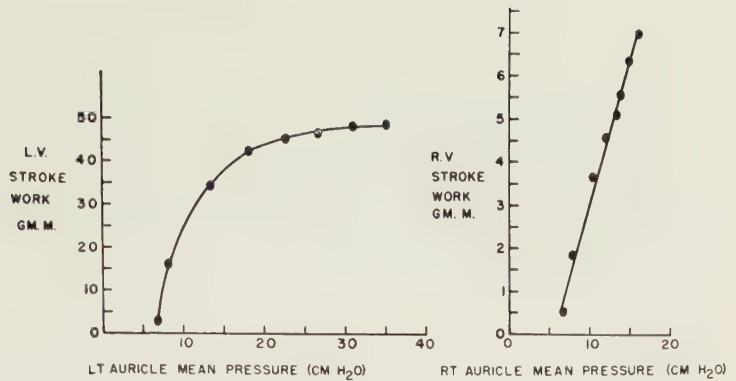


Fig. 2.—Relation between atrial pressure and stroke work in dog. (After SARNOFF & BERGLUND 1954).

energy developed by the heart muscle in order to force the blood through the pulmonary circulation.

Long-Term Effects of IPPV

An increase in the intrathoracic pressure initiates changes in the distribution of the body fluids (BARACH et al. 1946, 1947), in the urinary output (DRURY et al. 1947, HENRY & PEARCE 1956), in the sodium excretion (GETT et al. 1971) and in other mechanisms which may compensate for the circulatory changes primarily excited.

One of the objects of the investigation presented here was to study how rapidly circulatory changes occur, and to see if some compensatory mechanisms are excited within the first few minutes after such changes. The long-term mechanisms will not be discussed in this study.

MATERIAL AND METHODS

Four healthy mongrel dogs, weighing from 5.5 to 9.0 kg, were anaesthetized with an intravenous injection of pentobarbital, 50 mg/kg. After endotracheal intubation with cuffed Magill tube, the animals were ventilated with air. Muscular relaxation was obtained with diallyl-bis-nor-toxiferine, initially 1 mg/kg. Maintenance doses were given as required.

The ventilation was checked by P_{aO_2} , P_{aCO_2} and pH determinations with micro-

electrodes at 37° C. (Eschweiler and Co., Kiel; Radiometer, Copenhagen).

The mean levels were as follows: P_{aCO_2} 35.8 mm Hg (SD 7.0; n 29); P_{aO_2} 73.7 mm Hg (SD 11.6; n 29); pH 7.318 (SD 0.115; n 16).

The animals were ventilated with the prototype of a recently designed ventilator (INGELSTEDT et al. 1972). A frequency of 10 or 20 cpm was used. The minute volumes ranged from 1.6 to 3.0 l. The insufflation was given with a constant flow for 20 to 33 % of the entire respiratory cycle, with or without an EIP representing 20 % of the respiratory cycle. Rigid tubes were used between the ventilator and the experimental animal. The compressible volume of the ventilator and tubes was about 700 ml.

The body temperature of the animal was maintained at the normal level by warming the operating table. The anaesthetized dog was placed in the dorsal position, and after exposure of vessels in a femoral fold, a catheter was passed up into the right atrium and another into the abdominal aorta.

A left-sided thoracotomy was performed in the fourth interstice. The pericardium was split, care being taken to preserve the phrenic nerve. The main trunk of the pulmonary artery or the aortic root was dissected free, and an implantable transducer for electromagnetic blood-flow measurements was placed over the vessel.

Catheters were introduced into the left

atrium through the auriculum, and into the pulmonary artery through the infundibulum of the right ventricle.

The thoracotomy was closed, as a pleural drain with continuous suction at a negative pressure of 15 cm H₂O was established. Heparin was given in a dose of 150 I.U./kg. Glycose solution, 5.5 %, was administered intravenously at a rate of 2 ml/kg/hour.

Registration

During the experiments, the pressures in the right atrium, pulmonary artery, left atrium and aorta were recorded through polyethylene catheters (PE 160), 100 cm in length, by pressure transducers (Elema-Schönander EMT 34) connected to amplifiers (EMT 31) (Fig. 3). Calibration was performed against water columns of known heights. The site of entry of the vena cava into the right atrium was used as the zero level. Mean pressures were obtained by electrical integration in the amplifier and by planimetric integration.

The cardiac output was measured in the pulmonary artery or the aorta by means of electromagnetic flow meters (Nycotron 372-PC) by the technique described by KUGELBERG (1967). The calibration was checked with the saline flow through an isolated aorta preparation. The mean flow and momentary flow were recorded together with the pres-

ures and ECG on an 8-channel recorder (Elema-Schönander EMT 81). The stroke volume and mean pressures for the individual heartbeats were integrated from the momentary flow curve by a planimeter. The ventilatory function was checked by measurements of the gas flow by a pneumotachograph (Fleisch No. 2) (transducers and amplifiers EMT 34, EMT 31), and the tidal volume was measured by electrical integration of this signal. The calibration was performed with a piston operated by a synchronous motor. The oesophageal pressure was recorded through a catheter (PE 205), 60 cm in length, provided with a 4 cm long latex balloon placed midway down the oesophagus. This balloon was insufflated with 0.15 ml air.

The pressure at the distal end of the tracheal tube was measured through a catheter (PE 205), 60 cm in length. The ventilatory parameters were recorded on a second recorder (EMT 81).

During continuous registration of the circulation and ventilatory functions, the ventilatory pattern was changed after periods of from 2 to 30 minutes.

In two of the dogs, hypotension was induced during the latter part of the experiment by alpha-receptor blockade after administration of dibenoxamine, 1 and 2 mg/kg, respectively. The arterial mean pressure was 110–120 mm Hg before and 60–70 mm Hg after the blockade.

Calculations

The stroke work of the right ventricle was calculated according to the formula: –

$$SW_{RV} = SV_{RV} (\bar{P}_{pulm.art} - \bar{P}_{r.atr}).$$

and of the left ventricle according to the formula: –

$$SW_{LV} = SV_{LV} (1.36 \times \bar{P}_{art} - \bar{P}_{l.atr}).$$

In clinical practice, the term “resistance” (R) is used for the vascular resistance, while the concept of conductance (G), i.e. conducting capacity, is commonly used in the physiological literature. The relation between the two factors is $G = 1/R$. The conductance

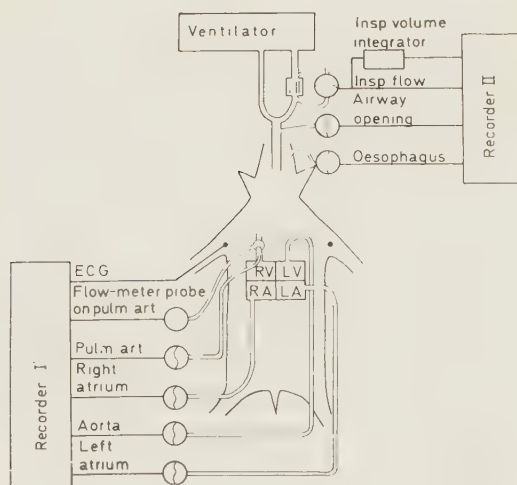


Fig. 3.—Experimental arrangement.

Fig. 4.—Frequency 20 cpm. Tidal volume 16 ml/kg. Insufflation time 20 %, EIP 0 and 20 % of respiratory cycle; change at arrow.

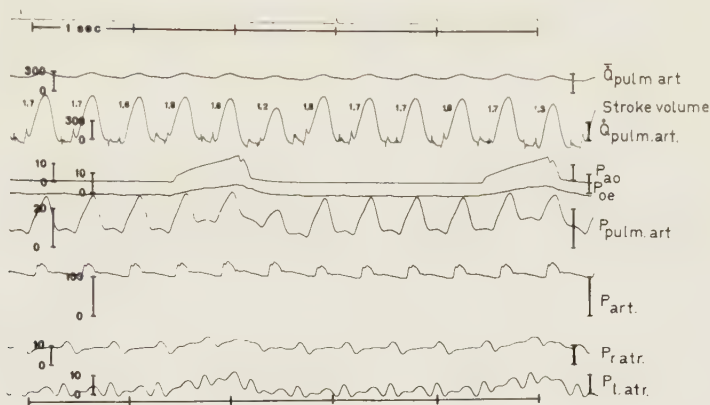
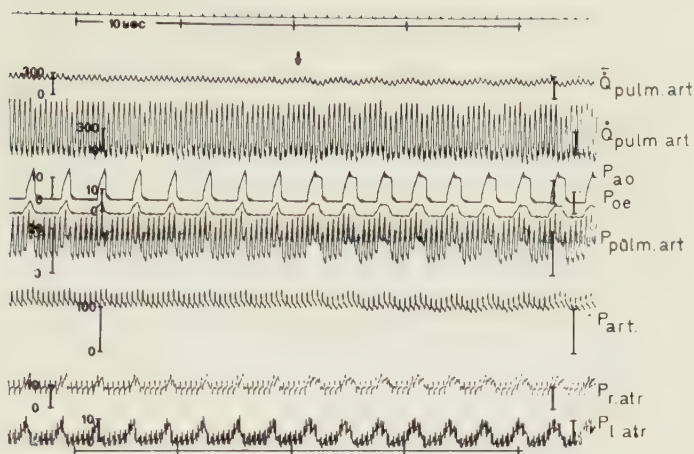


Fig. 5.—Frequency 20 cpm. Tidal volume 16 ml/kg. Insufflation time 20 %.

of the pulmonary circulation was calculated as

$$G_{\text{pulm}} = \frac{\bar{Q}}{\bar{P}_{\text{pulm.art}} - \bar{P}_{\text{l.atri}}} \text{ (ml/min)/cm H}_2\text{O}$$

and that of the systemic circulation as

$$G_{\text{syst}} = \frac{\bar{Q}}{1.36 \times \bar{P}_{\text{art}} - \bar{P}_{\text{r.atri}}} \text{ (ml/min)/cm H}_2\text{O}$$

When calculating the momentary changes, mean values for pressure and flowrate during each heartbeat were used. Effects of EIP on mean values for circulatory parameters were calculated from pressures and flowrates over 12 seconds, i.e. 2 or 4 complete respiratory cycles.

Alveolar pressure was measured from recordings of airway opening pressure, at mo-

ments of zero flow, and estimated between these moments.

The statistical mean values and the analyses of statistical significance according to Student's t-test were calculated by a computer (Olivetti Programma 101).

RESULTS

Momentary Effect of the Respiratory Cycle on Stroke Volume and Pressure

Fig. 4 shows the haemodynamic parameters in an anaesthetized dog with stable circulation and closed chest, with and without EIP.

Variations in pressure and flow occur synchronously with the ventilation, as indicated by the pressures in the airway and oesophagus. The pressures in the left and right atria and in the pulmonary artery largely follow the

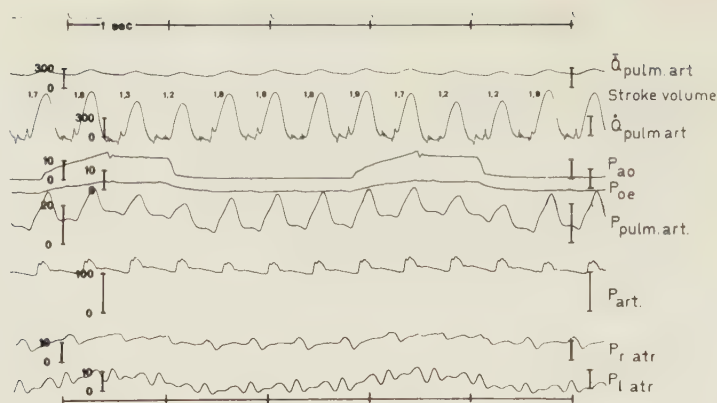


Fig. 6.—As Fig. 5. EIP 20 % added.

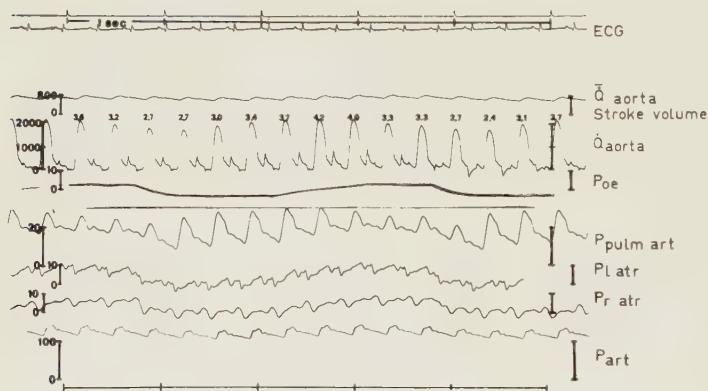


Fig. 7.—Frequency 20 cpm. Tidal volume 20 ml/kg. Insufflation time 33 %, EIP 20 %. ($P_{l,atr}$ from a registration some minutes later differs slightly in heart rate).

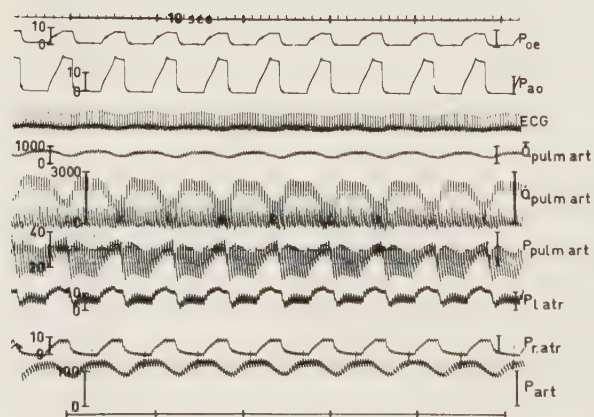


Fig. 8.—Ventilatory frequency 10 cpm. Tidal volume 40 ml/kg. Insufflation time 25 %. EIP 20 %.



Fig. 9.—Ventilatory frequency 10 cpm. Tidal volume 30 ml/kg. Insufflation time 25 %. EIP 20 %.

changes in the intrathoracic pressure, represented by the oesophageal pressure. The pulmonary flow decreases somewhat at the end of the insufflation, and the aortic pressure decreases one or two heartbeats later. The flow changes become more pronounced after adding an EIP, 20 % of the respiratory cycle.

In records taken at a higher paper speed, certain details can be distinguished (Fig. 5). When air is insufflated into the lungs the pulse amplitude of the pulmonary artery is reduced, and so is the stroke volume of the

right ventricle after about 0.5 second. During expiration, the stroke volume of the right ventricle is increased after about 0.5 second. At the same ventilation, but with added EIP, the stroke volume of the right ventricle is reduced for a longer period (Fig. 6). The outflow of the left ventricle and the arterial pressure increase during the initial phase of insufflation, and decrease during the initial phase of expiration (Fig. 7).

At a low ventilatory frequency and large tidal volumes more pronounced variations in

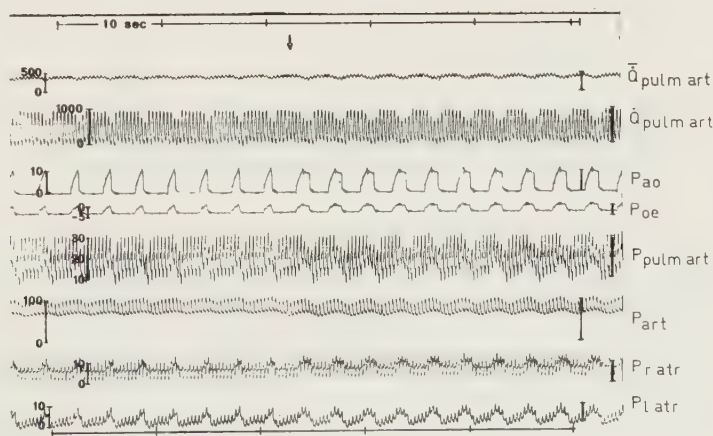


Fig. 10.—Ventilatory frequency 20 cpm. Tidal volume 15 ml/kg. Insufflation time 20 %. EIP 0 and 20 %; change at arrow. Induced hypotension (dibenzoxamine).

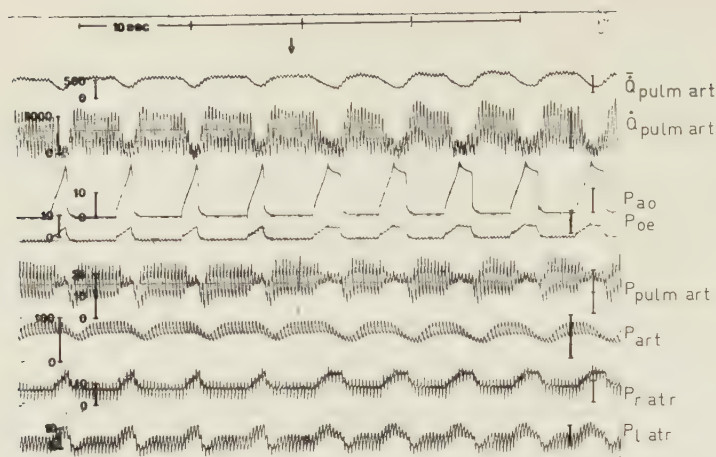


Fig. 11.—Ventilatory frequency 10 cpm. Tidal volume 31 ml/kg. Insufflation time 25 %. EIP 0 and 20 %; change at arrow. Induced hypotension (dibenoxamine).

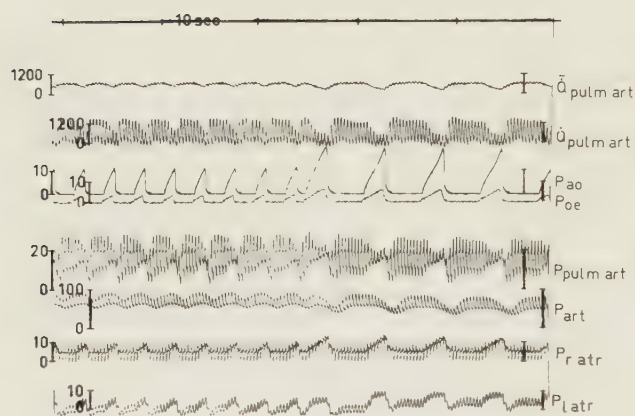


Fig. 12.—Ventilatory frequency 20 cpm and 10 cpm. Tidal volume 16, resp. 32 ml/kg. Insufflation time 33 %. Induced hypotension (dibenoxamine).

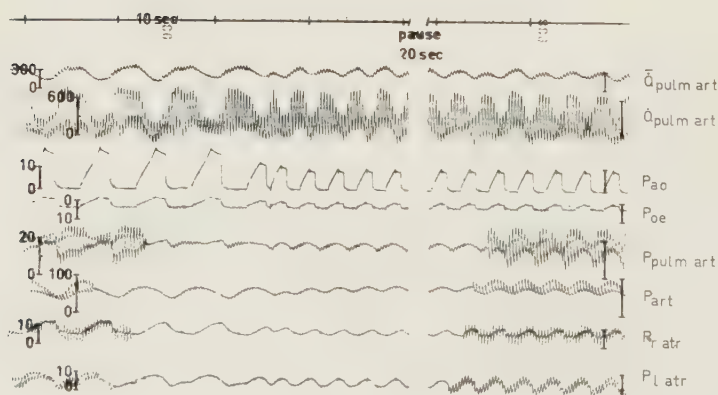


Fig. 13.—Ventilatory frequency 10 cpm and 20 cpm. Tidal volume 32, resp. 16 ml/kg. Insufflation time 33 %. EIP 20 %. Induced hypotension (dibenoxamine). (Mean pressure in the middle of the four lower tracings).

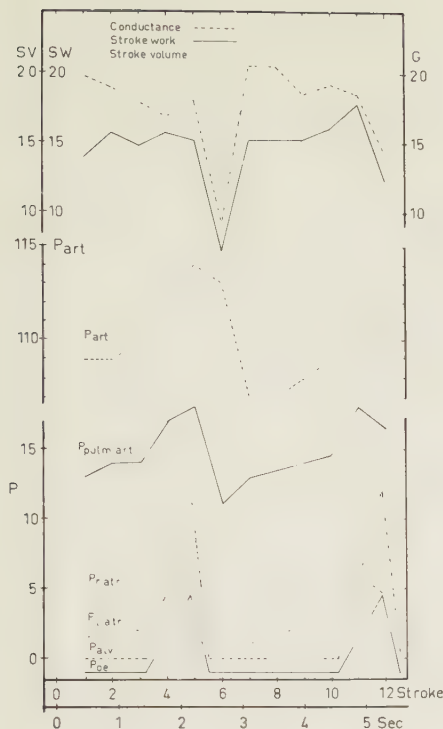


Fig. 14.—Beat-to-beat analysis of mean pressures, right ventricular stroke volume, work and pulmonary vascular conductance. Ventilatory frequency 20 cpm. Tidal volume 16 ml/kg. Insufflation time 25 %.

flow and pressure occur (Figs. 8 and 9). The pulse amplitude in the pulmonary artery is reduced during the initial phase of insufflation at unchanged stroke volumes, and it is vigorously increased at the beginning of expiration in spite of relatively small stroke volumes.

After alpha-receptor blockade by dibenexamine the flow variations increase to some extent (Fig. 10); they become very pronounced at a low ventilatory frequency with or without EIP (Fig. 11).

At unchanged minute volume, a change to a lower ventilatory frequency results in a lower arterial pressure and a lower pulmonary flow (Figs. 12 and 13; see also Table 4).

The circulatory changes begin immediately on the change in the ventilatory pattern, and a new level is reached after a few breaths.

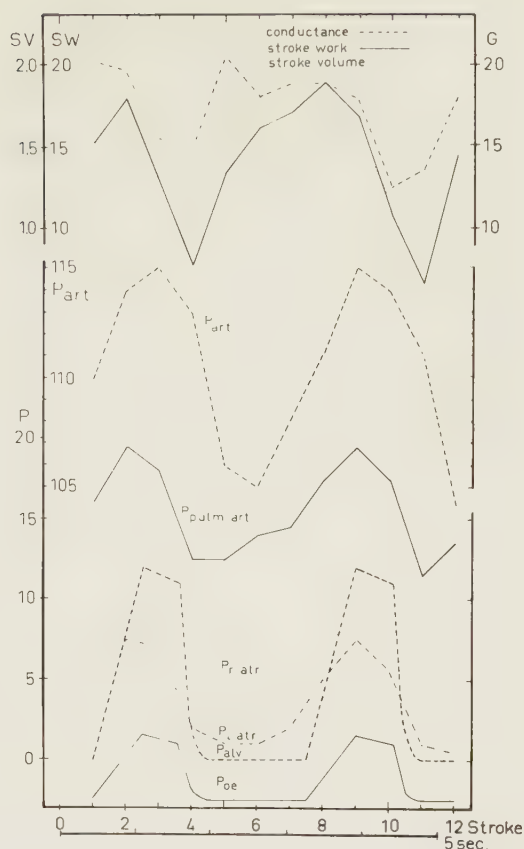


Fig. 15.—As Fig. 14. EIP 20 % added.

The Momentary Effect of the Respiratory Cycle on the Right Ventricular Stroke Work and Pulmonary Conductance

About 0.5 second after the start of insufflation, the stroke volume and stroke work of the right ventricle as well as the pulmonary conductance begin to fall. During expiration, these parameters return to their initial levels (Fig. 14).

When an EIP, 20 % of the respiratory cycle, is added, the decrease in stroke volume, stroke work and conductance becomes more protracted (Fig. 15). At a ventilatory frequency of 10 cpm (Fig. 16), plateaus for stroke volume, stroke work and conductance are established towards the end of expiration, and a slight "overshoot" can be distinguished in the curves for stroke volume and stroke work

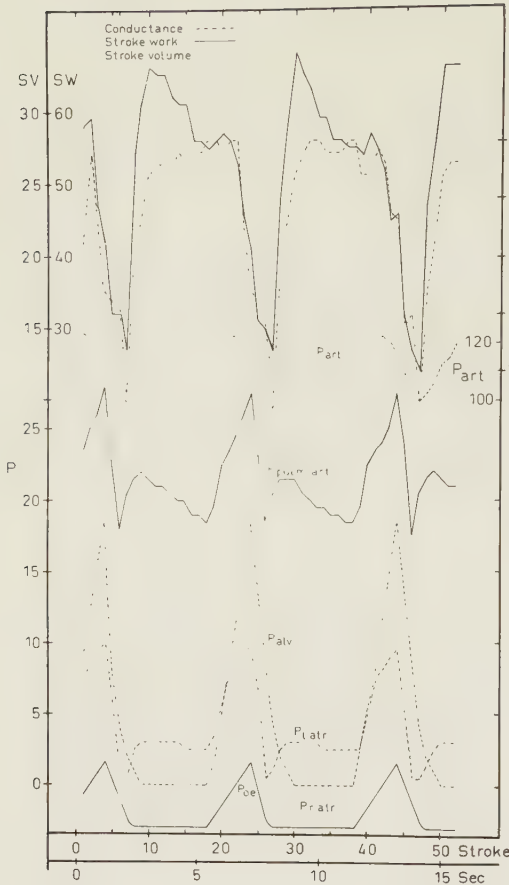


Fig. 16.—Beat-to-beat analysis of mean pressures, right ventricular stroke volume, work and pulmonary vascular conductance. Ventilatory frequency 10 cpm. Tidal volume 40 ml/kg. Insufflation time 25 %.

during the initial phase of expiration. The curve for the pulmonary conductance here shows some deviation from that for the stroke volume. When an EIP is added, a plateau is established even during the inspiratory phase (Fig. 17).

At a frequency of 20 cpm, alpha-receptor blockade is followed by a somewhat more pronounced fall in stroke volume and, particularly, in stroke work (Fig. 18). At a frequency of 10 cpm, alpha-receptor blockade gives only a slight overshoot in the curves for stroke volume and stroke work (Fig. 19) compared to non-blocked state (Fig. 16).

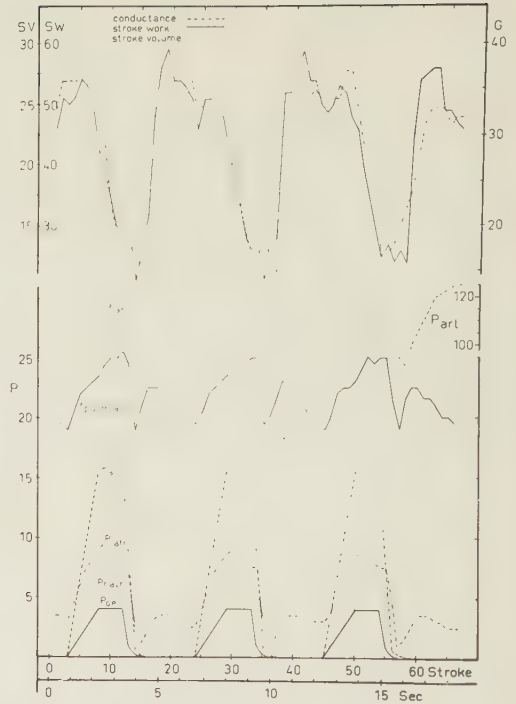


Fig. 17.—As Fig. 16. EIP 20 % added.

Momentary Effect of the Respiratory Cycle on the Left Ventricular Stroke Volume and Stroke Work

The stroke volume and stroke work of the left ventricle are related to the respiratory cycle as is shown in Fig. 20. These parameters are synchronously related and reach their maxima in the beginning of the inspiratory phase and their minima in the beginning of the expiratory phase.

Effect of EIP on the Mean Values of Pressures, Cardiac Output, Right and Left Ventricular Stroke Work and on the Conductance of the Pulmonary and Systemic Circulations

Under the experimental conditions used, the addition of an EIP, 20 % of the respiratory cycle, at a frequency of 20 cpm gave an increase in the intra-alveolar mean pressure of 2.2 ± 0.1 cm H₂O.

Measurements performed 20 seconds and 2 minutes after the addition of an EIP showed an increase in the pressures in the right and

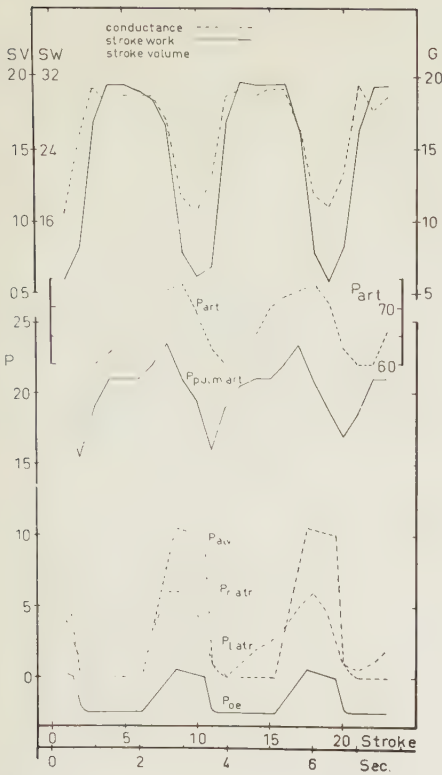


Fig. 18.—Beat-to-beat analysis of mean pressures, right ventricular stroke volume, work and pulmonary vascular conductance. Ventilatory frequency 20 cpm. Tidal volume 15 ml/kg. Insufflation time 25 %, EIP 20 %. Induced hypotension (dibenzamine).

left atria and in the pulmonary artery of the same order of magnitude as that in the oesophagus. Furthermore, slight falls occurred in the arterial pressure, cardiac output, stroke work of the right and left ventricles and in the conductance of the pulmonary circulation, while the heart rate and the conductance of the systemic circulation were unchanged (Fig. 21 and Table 1).

On the removal of the EIP, corresponding results were obtained, but in the opposite direction.

A comparison of the values at 20 seconds and 2 minutes after the change in the ventilatory pattern shows no significant changes in any of the parameters analysed.

Measurements performed during alpha-re-

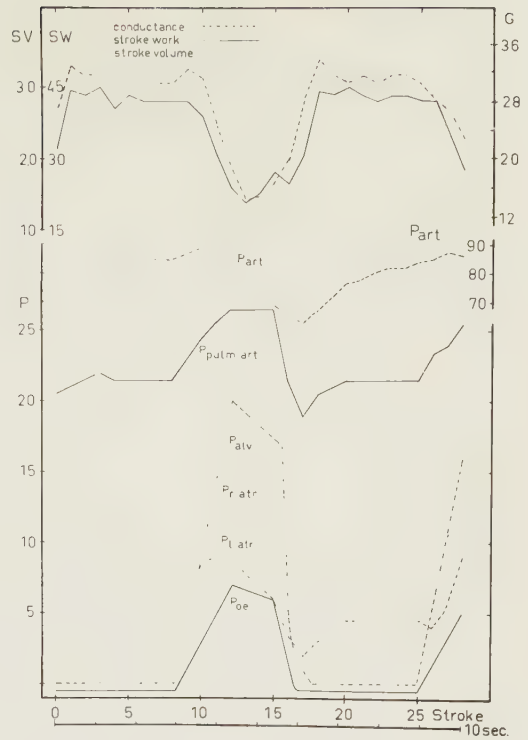


Fig. 19.—Beat-to-beat analysis of mean pressures, right ventricular stroke volume, work and pulmonary vascular conductance. Ventilatory frequency 10 cpm. Tidal volume 30 ml/kg. Insufflation time 25 %, EIP 20 %. Induced hypotension (dibenzamine).

ceptor blockade showed that the addition of an EIP, 20 % of the respiratory cycle, at a ventilatory frequency of 20 cpm led to an increase in the intra-alveolar mean pressure of 2.2 ± 0.2 cm H₂O.

The increases in the pressures in the right and left atria were of the same order of magnitude as those in the oesophagus (Fig. 22 and Table 2). No increase in pressure occurred in the pulmonary artery. The arterial pressure, cardiac output, the stroke work of the right and left ventricles as well as the conductance of the pulmonary circulation decreased, while the heart rate increased. A slight increase was seen in the conductance of the systemic circulation.

On the removal of the EIP, corresponding

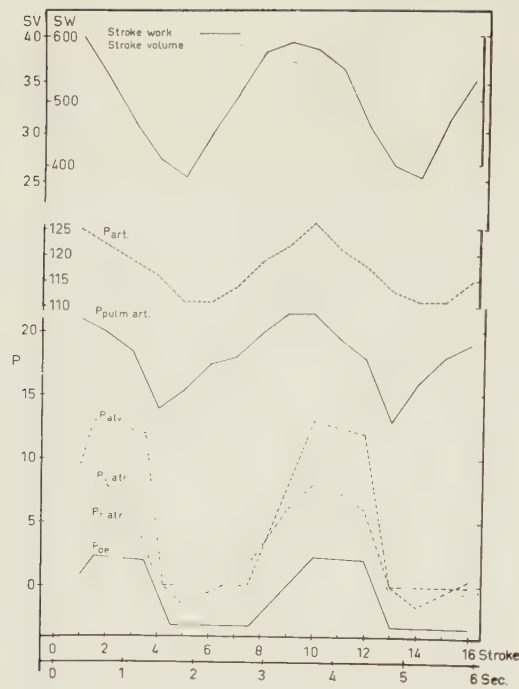


Fig. 20.—Beat-to-beat analysis of mean pressures and left ventricular stroke work. Ventilatory frequency 20 cpm. Tidal volume 20 ml/kg. Insufflation time 33 %, EIP 20 %.

Table 1.
Insp. 20%. 20 cpm. Effect of EIP, 20% of respiratory cycle.

	P oesophagus			P right atrium			P pulmonary artery			P left atrium			P artery			Cardiac output		
	Con- trol	After 20 sec	After 2 min	Con- trol	After 20 sec	After 2 min	Con- trol	20 sec	2 min	Con- trol	20 sec	2 min	Con- trol	20 sec	2 min	Con- trol	20 sec	2 min
	2.3	3.0	3.5	7.5	8.0	8.5	12.0	12.5	12.5	2.5	3.0	3.0	114	110	110	235	220	215
	2.7	3.7	3.5	8.0	9.0	9.0	13.5	14.0	14.5	2.5	3.0	2.5	112	110	109	225	210	215
	2.5	3.3	3.2	8.5	9.0	9.5	14.0	14.5	15.0	3.5	3.5	3.5	111	106	106	215	210	210
	2.7	3.2	3.0	9.0	10.0	10.0	15.0	16.0	15.0	2.5	3.0	2.5	112	107	108	230	215	230
	2.0	3.0	2.7	8.5	9.5	9.5	14.0	15.0	15.0	2.0	2.5	3.0	113	113	113	220	215	215
	1.8	2.7	2.7	9.5	10.0	10.0	15.0	15.5	15.5	2.0	2.5	2.5	115	114	110	230	220	210
M	2.3	3.2	3.1	8.5	9.3	9.4	13.9	14.6	14.6	2.5	2.9	2.8	113	110	109	226	215	216
SD	0.4	0.3	0.4	0.7	0.8	0.6	1.1	1.2	1.1	0.5	0.4	0.4	1.5	3.2	2.3	3.4	4.5	7.4
t-value and significance																		
C-20 sec	10.31***			6.71**			6.32**			4.99**			3.25*			5.40**		
C-2 min	6.38**			10.98***			4.00*			2.00-			4.58**			2.93*		
20 sec- 2 min	0.43-			1.58-			0-			0.54-			0.93-			0.24-		

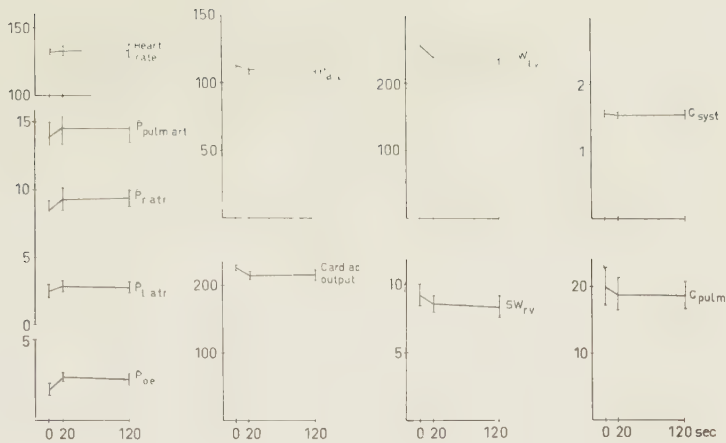


Fig. 21.—Circulatory parameters before, 20 seconds and 2 minutes after addition of EIP 20 %. Respiratory frequency 20 cpm. Mean value and SD of 6 observations. See figures in Table 1.

DISCUSSION

The Momentary Effect on Pressure and Stroke Volume

Experiments with continuous blood-flow measurements in the study of the effect of IPPV in animals with a closed chest have previously been published by BRECHER & HUBAY (1955) who measured the flow in the

vena cava and the pulmonary artery; by MORENO et al. (1967), MORGAN et al. (1966 b, 1967, 1969) and ABEL & WALDHAUSEN (1968, 1969) who measured the flow in the vena cava and aorta; and by MORGAN et al. (1966 a, 1968) who measured the flow in the vena cava, pulmonary vein, pulmonary artery and aorta.

The results of the investigation reported

Heart rate			Stroke work right ventricle			Conductance pulm. circ.			Stroke work left ventricle			Conductance syst. circ.		
Control	20 sec	2 min	Control	20 sec	2 min	Control	20 sec	2 min	Control	20 sec	2 min	Control	20 sec	2 min
133	130	127	7.95	7.62	6.77	24.7	23.2	22.6	269	249	249	1.60	1.56	1.52
128	128	130	9.67	8.20	9.10	20.5	19.1	17.9	263	242	241	1.56	1.50	1.55
131	131	130	9.03	8.82	8.89	20.5	19.1	18.3	243	225	226	1.51	1.56	1.56
135	135	134	10.22	9.56	8.58	18.4	16.5	18.4	255	227	247	1.61	1.60	1.69
133	135	137	9.10	8.76	8.63	18.3	17.2	17.9	250	240	237	1.51	1.49	1.49
133	136	138	9.51	8.90	8.37	17.0	16.9	16.2	266	246	223	1.57	1.53	1.51
132	133	133	9.25	8.64	8.39	19.9	18.7	18.6	258	238	237	1.56	1.54	1.55
2.4	3.3	4.4	0.77	0.66	0.83	2.8	2.5	2.1	10.1	9.9	10.7	0.04	0.04	0.07
0.40-			3.22*			4.94**			8.25***			1.31-		
0.30-			3.78**			3.05*			4.15**			0.27-		
0.67-			0.89-			0.24-			0.18-			0.67-		

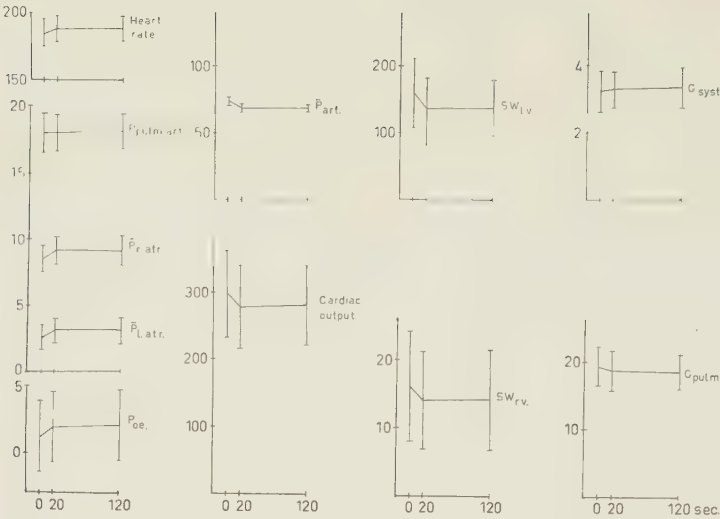


Fig. 22.—Circulatory parameters before, 20 seconds and 2 minutes after addition of EIP 20 %. Respiratory frequency 20 cpm. Induced hypotension (dibenoxamine). Mean value and SD of 17 observations. See figures in Table 2.

Table 2.
Insp. 20 and 33%, 20 cpm. Induced hypotension. Effect of EIP, 20% of respiratory cycle.

	P oesophagus			P right atrium			P pulmonary artery			P left atrium			P artery			Cardiac output		
	Control	After 20 sec	After 2 min	Control	After 20 sec	After 2 min	Control	20 sec	2 min	Control	20 sec	2 min	Control	20 sec	2 min	Control	20 sec	2 min
	2.8	3.2	3.2	7.0	7.5	7.5	20.0	20.0	20.5	3.0	3.5	3.5	82	76	72	420	396	396
	2.2	2.8	2.6	7.5	7.5	7.0	20.5	20.5	20.5	3.0	3.5	3.0	77	72	70	420	372	396
	2.0	2.6	3.2	7.5	7.5	8.0	19.5	19.5	19.0	2.0	3.0	2.5	76	73	71	396	360	360
	2.8	3.6	3.8	7.0	8.0	7.5	18.5	18.0	18.0	1.5	2.0	1.0	73	70	69	384	378	354
	3.6	4.6	5.4	8.0	8.5	9.5	17.5	17.5	17.0	0.5	1.0	1.0	74	69	71	342	336	330
	0.4	1.2	1.2	8.0	8.5	9.5	16.0	17.0	18.0	3.0	3.5	3.5	76	68	71	260	230	270
	-2.2	-1.4	-1.4	9.0	9.0	9.0	18.0	18.0	18.0	3.0	3.0	4.0	74	69	69	270	260	250
	-2.2	-1.4	-1.4	8.0	9.0	9.0	18.5	18.5	18.0	3.0	3.5	3.5	71	67	67	270	245	250
	-2.0	-1.2	-1.2	8.5	9.0	9.0	18.5	18.5	18.5	2.5	3.0	3.5	70	65	66	265	250	250
	-2.2	-1.4	-1.4	8.5	9.5	9.0	19.0	19.0	19.0	2.0	2.5	3.0	70	64	65	270	240	250
	-2.2	-1.4	-1.4	9.0	9.5	9.5	18.5	18.5	19.0	2.0	2.5	2.5	70	64	63	260	240	240
	-2.2	-1.4	-1.4	9.0	10.5	10.0	19.5	19.5	19.0	2.0	3.0	2.5	72	68	65	285	275	265
	2.6	3.2	3.4	10.0	10.0	9.0	16.5	16.5	16.5	4.0	5.0	5.0	75	69	68	270	240	228
	3.4	4.4	4.2	9.0	9.5	10.0	16.0	16.5	17.0	3.5	4.0	4.0	74	69	69	240	216	240
	4.0	4.4	4.8	9.5	10.0	10.5	17.0	16.5	16.5	3.5	4.0	3.5	74	68	69	237	240	246
	4.0	4.8	4.8	10.0	10.5	11.0	16.0	16.5	16.5	3.5	3.5	3.5	74	67	68	240	216	210
	4.6	5.0	5.2	9.5	10.0	10.0	16.0	16.0	16.5	2.5	3.0	3.0	71	64	67	234	240	234
M	1.1	1.9	2.0	8.5	9.1	9.1	18.0	18.0	18.1	2.6	3.1	3.1	73.7	68.4	68.1	298	278	281
SD	2.7	2.6	2.7	1.0	1.0	1.1	1.5	1.4	1.3	0.9	0.9	1.0	3.1	3.3	2.5	66	62	60
t-value and significance																		
C-20 sec	15.76***			5.28**			0.70-			7.86***			16.15***			5.62***		
C-2 min	11.11***			3.78**			0.72-			4.70***			13.27***			4.84***		
20 sec-2 min	1.83-			0.31-			0.57-			0.52-			0.25-			0.55-		

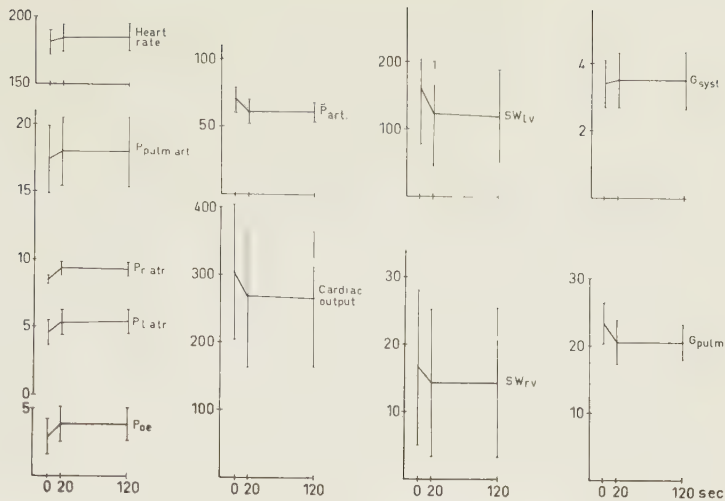


Fig. 23.—Circulatory parameters before, 20 seconds and 2 minutes after addition of EIP 20 %. Respiratory frequency 10 cpm. Induced hypotension (dibenoxamine). Mean value and SD of 6 observations. See figures in Table 3.

Heart rate			Stroke work right ventricle			Conductance pulm. circ.			Stroke work left ventricle			Conductance syst. circ.		
Control	20 sec	2 min	Control	20 sec	2 min	Control	20 sec	2 min	Control	20 sec	2 min	Control	20 sec	2 min
170	170	172	32.1	29.1	29.9	24.7	24.0	23.3	269	231	216	4.01	4.16	4.41
171	172	174	31.9	28.1	30.7	24.0	21.9	22.6	251	203	211	4.35	4.15	4.48
172	174	176	27.6	24.8	22.5	22.6	21.8	21.8	232	200	192	4.16	3.95	4.07
174	176	177	25.4	21.5	21.0	22.6	23.6	20.8	216	202	185	4.15	4.34	4.13
178	180	180	18.2	16.8	13.8	20.1	20.4	20.6	193	173	175	3.70	3.92	3.79
190	191	193	10.9	10.2	11.9	20.0	17.0	18.6	138	106	129	2.73	2.73	3.10
190	190	196	12.8	12.3	11.5	18.0	17.3	17.9	139	125	114	2.96	3.08	2.96
191	197	193	14.8	11.8	11.7	17.4	16.3	17.2	133	108	113	3.05	3.00	3.06
196	197	197	13.5	12.1	12.1	16.6	16.1	16.7	125	109	109	3.04	3.17	3.12
195	200	199	14.5	11.4	12.6	15.9	14.5	15.6	128	101	108	3.10	3.10	3.17
198	200	200	12.5	10.8	11.4	15.8	15.0	14.5	121	101	100	3.04	3.10	3.15
200	199	200	15.0	12.4	11.9	16.3	16.7	16.1	136	124	113	3.22	3.37	3.42
181	185	186	9.7	8.4	9.2	21.6	20.9	18.2	146	115	108	2.96	2.89	2.75
184	188	187	9.1	8.0	9.0	19.2	17.3	18.5	126	103	115	2.63	2.56	2.89
186	191	189	9.6	8.2	7.8	17.6	19.2	18.7	123	111	117	2.60	2.94	2.97
188	190	190	7.7	6.8	6.1	19.2	16.6	16.0	123	99	98	2.67	2.69	2.57
187	190	190	8.1	7.6	8.0	17.3	18.5	17.3	117	106	109	2.69	3.15	2.82
185	188	188	16.1	14.1	14.2	19.3	18.7	18.5	160	136	136	3.24	3.31	3.34
10	10	9	8.1	7.3	7.4	2.9	2.9	2.5	51	45	41	0.60	0.57	0.60
4.82***			7.03***			2.20*			9.37***			1.70-		
8.17***			4.70***			2.93**			7.52***			2.53*		
1.03-			0.14-			1.09-			0.18			0.68-		

Table 3.
Insp. 20 and 33 %, 10 cpm. Induced hypotension. Effect of EIP 20 % of respiratory cycle.

	P oesophagus			P right atrium			P pulmonary artery			P left atrium			P artery			Cardiac output		
	Con- trol	After 20 sec	After 2 min	Con- trol	After 20 sec	After 2 min	Con- trol	20 sec	2 min	Con- trol	20 sec	2 min	Con- trol	20 sec	2 min	Con- trol	20 sec	2 min
	4.5	5.5	5.3	8.5	9.5	9.0	21.0	22.0	22.0	4.0	4.5	4.5	82	71	71	432	408	408
	1.0	1.8	1.8	8.5	9.5	9.5	15.0	15.5	15.5	3.5	4.5	4.5	65	54	56	230	205	210
	4.0	4.7	4.5	8.0	8.5	8.5	20.0	20.0	20.5	4.0	4.5	5.0	78	74	69	432	396	372
	3.0	4.0	4.0	8.5	9.0	9.0	17.0	17.5	17.0	5.0	6.0	6.0	61	52	55	240	220	225
	2.0	3.0	3.2	8.5	9.5	9.5	16.0	16.5	16.5	6.0	6.5	6.5	69	57	57	252	195	195
	2.7	3.5	3.7	9.0	10.0	10.0	15.5	16.5	16.5	5.0	6.0	6.0	67	60	60	234	180	180
M	2.9	3.8	3.8	8.5	9.3	9.3	17.4	18.0	18.0	4.6	5.3	5.4	70.3	61.3	61.3	303	267	265
SD	1.3	1.3	1.2	0.3	0.5	0.5	2.5	2.5	2.5	0.9	0.9	0.9	8.0	9.1	6.9	100	105	99
t-value and significance																		
C-20 sec	16.28***			7.90***			3.80*			6.71**			7.27***			5.50**		
C-2 min	9.01***			6.71**			3.80*			7.91***			9.67***			4.53**		
20 sec-2 min	0.18-			1.00-			0-			1.00-			0-			0.52-		

Table 4.
Effect of change of ventilatory frequency between 20 and 10 cpm. Minute ventilation constant. Inspiration 20 or 33 %. EIP 0 or 20 % of respiratory cycle.

	P oesophagus		P right atrium		P pulm. artery		P left atrium		P artery		Cardiac output	
	20 cpm	10 cpm	20 cpm	10 cpm	20 cpm	10 cpm	20 cpm	10 cpm	20 cpm	10 cpm	20 cpm	10 cpm
	0.3	0.8	8.0	8.5	16.0	15.5	3.0	3.0	76	69	260	228
	0.3	1.1	7.5	8.5	18.5	18.0	3.0	4.0	68	61	300	260
	3.6	4.5	8.5	9.0	18.5	18.0	3.0	3.5	76	69	420	390
	2.8	3.6	9.5	10.0	16.0	16.5	5.0	6.0	72	60	258	185
	0.2	1.2	8.5	10.0	18.5	17.0	4.0	4.5	67	54	234	186
M	1.4	2.2	8.4	9.2	17.5	17.0	3.6	4.2	71.8	62.6	294	250
SD	1.6	1.7	0.7	0.8	1.4	1.1	0.9	1.2	4.3	6.4	74	84
t	9.57***		4.00*		1.58-		3.21*		6.78**		5.73**	

Heart rate			Stroke work right ventricle			Conductance pulm. circ.			Stroke work left ventricle			Conductance syst. circ.		
Con- trol	20 sec	2 min	Con- trol	20 sec	2 min	Con- trol	20 sec	2 min	Con- trol	20 sec	2 min	Con- trol	20 sec	2 min
169	171	171	32.0	29.8	31.0	25.4	23.3	23.3	275	221	221	4.18	4.69	4.69
189	195	197	7.9	6.3	6.4	20.0	18.6	19.1	103	73	77	2.87	3.21	3.15
170	172	173	30.5	26.5	25.8	27.0	25.6	24.0	259	222	190	4.41	4.28	4.34
182	187	190	11.2	10.0	9.5	20.0	19.1	20.5	102	75	81	3.21	3.60	3.45
188	190	188	10.1	7.2	7.3	25.2	19.5	19.5	117	73	73	2.94	2.87	2.87
186	188	188	8.2	6.2	6.2	22.3	17.1	17.1	108	72	72	2.87	2.55	2.55
181	184	185	16.7	14.3	14.4	23.3	20.5	20.6	161	123	119	3.41	3.53	3.51
9	10	10	11.4	10.9	11.0	3.0	3.2	2.6	83	77	68	0.70	0.83	0.84
	4.23**			5.65**			3.24*			9.48***			0.87-	
	2.79*			4.22**			2.77*			5.69**			0.91-	
	0.93-			0.12-			0.13-			0.64-			0.85-	

Heart rate		Stroke work right ventricle		Conductance pulm. circ.		Stroke work left ventricle		Conductance syst. circ.		
20 cpm	10 cpm	20 cpm	10 cpm	20 cpm	10 cpm	20 cpm	10 cpm	20 cpm	10 cpm	
190	193	10.9	8.3	20.0	18.2	109	83	2.73	2.66	Insp. 20%
181	182	18.2	13.6	19.4	18.6	182	136	3.56	3.48	EIP 0%
172	173	24.4	15.8	27.7	26.9	244	158	4.41	4.63	Insp. 33%
183	186	9.2	6.5	23.5	17.6	92	65	2.92	2.98	EIP 0%
190	190	12.3	6.9	16.1	14.9	123	69	2.82	2.97	Insp. 20%
										EIP 20%
183	185	15.0	10.2	21.3	19.2	150	102	3.29	3.34	Insp. 33%
7	8	6.3	4.2	4.4	2.0	63	42	0.71	0.78	EIP 20%
2.67-		4.36*		2.17		4.36*		0.95-		

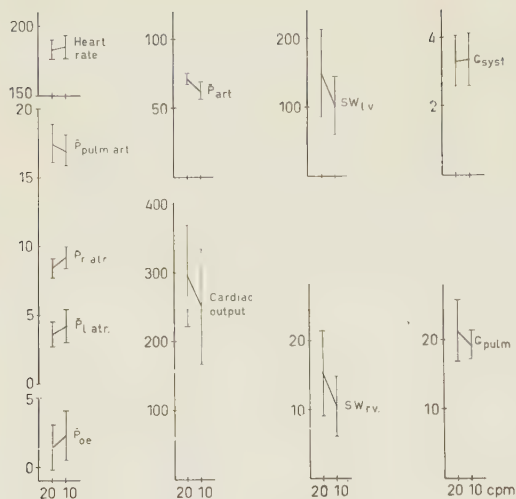


Fig. 24.—Circulatory parameters at respiratory frequencies 20 and 10 cpm, before and 20 seconds after change. Induced hypotension (dibenoxamine). Mean value and SD of 5 observations. See figures in Table 4.

here are in agreement with the descriptions of the flow in the aorta and pulmonary artery given by the above-mentioned authors.

The changes caused by an added EIP and their accentuation on alpha-receptor blockade at a low ventilatory frequency are in keeping with the generally accepted views on the effect of the intrathoracic pressure on the circulation (WERKÖ 1947, SARNOFF et al. 1948, OPIE et al. 1961, MUSHIN et al. 1969).

However, the discrepancies between the stroke volume of the right ventricle and the pulse amplitude of the pulmonary artery do not seem to have been reported in previous studies. Such discrepancies are seen in Fig. 9 and, to a certain extent, also in Figs. 5 and 6. They may be due to short-lived variations in the transmural pressure in the pulmonary artery, with changed compliance conditions, or to the fact that the pressure of the alveoli on the pulmonary capillaries gives a varying "Windkessel" effect. The elasticity and retraction of the pulmonary arteries may, on changes in the lung volume, also exert a certain influence.

Momentary Effects on the Right Ventricular Stroke Work

The stroke work of the right ventricle has not previously been used in the assessment of the effect of ventilation on the venous filling.

As a rule, the transmural pressure in the right ventricle or atrium is used, but this method is beset with certain limitations. The intraluminal pressure must be related to a zero value the biological correctness of which cannot be proved. The position of the heart is changed during the respiratory cycle (NORDENSTRÖM 1960), which affects the results of measurements, and extramural pressure of the heart is not exactly commensurate with the pleural pressure, which is often used to represent the extramural pressure. The elasticity, weight and inertia of the surrounding tissues also exert a certain influence on the measurements (WIGGERS et al. 1947, BROOKHART & BOYD 1947, COLERIDGE & LINDEN 1954, FAHRI et al. 1957, AGOSTONI & MISEROCCHI 1970). When the oesophageal pressure is used to represent the pleural pressure, the weight of fluid present in the oesophagus and the tonus of the oesophageal wall are other sources of error.

In the present investigation it was decided to use the oesophageal pressure as the representative of the pleural pressure. The oesophageal pressures measured give, however, some information on the pleural pressure, but they cannot be used for calculating the transmural pressure with sufficient accuracy. Instead, the correlation between the stroke work and filling pressure demonstrated by SARNOFF & BERGLUND (1954) was employed. The stroke work of the right ventricle was calculated from the stroke volume and the difference between the pressures in the artery and the atrium. If these pressures are given the same reference points, the exact difference can be measured without a biological zero level. Great changes in the heart rate are presumed to affect the relation between the atrial filling and the stroke work. However, in the experiments performed, deviations amounting to only a few per cent were observed during the various phases of the ven-

tilatory cycle. The correlation between the changes in stroke volume and stroke work observed (Figs. 14–19) is due to the fact that the pressure difference between the right ventricle and the pulmonary artery is essentially unaffected by the blood-flow variations during the ventilatory cycle. The formula for stroke work is:

$$SW_{rv} = SV_{rv} (\bar{P}_{pulm.art} - \bar{P}_{r.atr}).$$

$$\text{When } \bar{P}_{pulm.art} - \bar{P}_{r.atr} = k,$$

$$SW_{rv} = SV_{rv} \times k.$$

That the pressures in the right atrium and pulmonary artery approximately follow that in the pleural cavity is in agreement with previous observations (LENFENT & HOWELL 1960).

The parallel course of stroke volume and stroke work also implies that each millilitre of blood which is pumped through the pulmonary vessels requires an equal amount of cardiac work, although the flow and resistance in the pulmonary circulation vary in IPPV.

Momentary Effect on Pulmonary Conductance

The vascular conditions in the lung are not homogenous. Changes in the intrathoracic pressure affect arteries, capillaries and veins in a different way in the various regions of the lung. Of the greatest interest is the blood flow in the capillaries, which perform the actual function of the lung, viz. the gas exchange. The conductance of the various vascular regions cannot be demarcated, but the combined effect can be assessed. The value for the momentary conductance calculated by the formula used constitutes a summation of the flow and pressure conditions in the arteries, capillaries and veins, while only the flow in the pulmonary artery and the pressures in the pulmonary artery and the left atrium were measured. During insufflation the blood volume of the pulmonary capillaries are decreased. A corresponding increase in the blood volume occurs during expiration.

In the discussion of pulmonary conductance and pulmonary resistance it should be

noted that, strictly speaking, these concepts are not absolutely exact: "... as the result of the many different active and passive influences which may affect the relationship between $\Delta\bar{P}$ and $\bar{Q}$, the term 'resistance' is bereft of its original physical meaning: instead of representing a fixed attribute of blood vessels, it has assumed physiological meaning as a product of a set of circumstances" (FISHMAN 1963).

In view of the agreement between the pressures in the pulmonary artery and left atrium (Figs. 4–19) there must also be agreement between the curves for stroke volume and conductance of the pulmonary vascular system (Figs. 14–19).

$$G_{pulm} = \frac{SV_{rv}}{\bar{P}_{pulm.art} - \bar{P}_{l.atr}}.$$

$$\text{When } \bar{P}_{pulm.art} - \bar{P}_{l.atr} = k, G_{pulm} = \frac{SV_{rv}}{k}.$$

The observation that the pressures in the pulmonary artery and vein at positive airway pressure approximately follow the pleural pressure is in agreement with the results of previous studies (HAMILTON 1939, LENFENT & HOWELL 1960).

Thus, good agreement exists between the curves for stroke volume, conductance and right ventricular stroke work. On limited changes in the filling pressure in the right atrium, this pressure seems to show an approximately linear relation to the right ventricular stroke work (SARNOFF & BERGLUND 1954, SARNOFF 1955, ETSTEN & LI 1960, SHIMASOTO et al. 1963).

The conclusion is that a time relation and an approximately quantitative relation exists between the filling pressure of the right heart and the conductance of the pulmonary vascular system under the experimental condition used in the present investigation. The intrathoracic pressure exerts its influence with the same inertia on the two fluid systems which the intrathoracic veins and pulmonary vessels constitute.

It has been discussed whether the circulatory inhibitions on insufflation of the lungs are primarily due to an inhibition of the ven-

ous return (HUMPREYS et al. 1938, WERKÖ 1947, MORGAN et al. 1966 b) or rather to an increased pulmonary resistance (BEECHER et al. 1943, BARACH et al. 1946, HUBAY et al. 1955, ANDERSEN & KUCHIBAK 1967).

It is unnecessary to range these phenomena in a certain order. They should rather be interpreted as two functions balanced in such a way that the pressure in the pulmonary artery and the arteriovenous pressure difference are stabilised when rapid changes in the intrathoracic pressure occur.

In the present investigation, this applies both to the momentary changes during ventilation (Figs. 14–19) and to the changes in the mean pressure on the addition of an EIP (Figs. 21–24). This balance between flow and conductance may contribute to a certain measure of stabilisation of the pulmonary capillary blood flow distribution in spite of the flow variations which occur on rapid changes in the intrathoracic pressure. This investigation revealed distinct exceptions to this balance only in the presence of a severely deranged circulation. The pressure in the pulmonary artery then falls during the early insufflatory phase, apparently because the atrial filling is affected earlier or more vigorously than the pulmonary conductance. Under the experimental conditions used, only relatively small pressure changes were studied. Whether similar relations exist on greater pressure changes, or in general, cannot be assessed on the basis of the experiments performed.

The Effect of the Respiratory Cycle on the Stroke Work of the Left Ventricle

In analogy with the functions of the right heart, the stroke work of the left ventricle reflects the filling of the left atrium. The stroke volume and stroke work show also here both a time relation and a quantitative relation to an increase during the insufflatory phase (Fig. 6), and the lowest value occurs in the initial phase of the expiration. Just like the right ventricle, the left ventricle performs a certain amount of work millilitre of blood, independent of the variations in stroke volume.

The Effect of EIP on Mean Pressure, Cardiac Output, Stroke Work and Conductance

The primary object of the experiments performed was to study to what extent EIP affected the circulation. Previous studies have shown that even moderate changes in the intrathoracic pressure give rise to a measurable influence on the circulation. In addition, barbiturate anaesthesia causes a certain diminution of the circulatory reflexes, and muscular relaxation increases the possibility of blood-volume fluctuations in the abdominal vessels.

In the experiments performed, it was observed that an increase in the alveolar mean pressure of about 2 cm H₂O causes a slight decrease in cardiac output and arterial pressure in dogs with otherwise intact circulation and healthy lungs. However, these changes are so slight that they are definitely without any importance for the general condition of the experimental animals.

It was ascertained that blockade of the circulatory reflexes results in increased susceptibility to changes in the intrathoracic pressure.

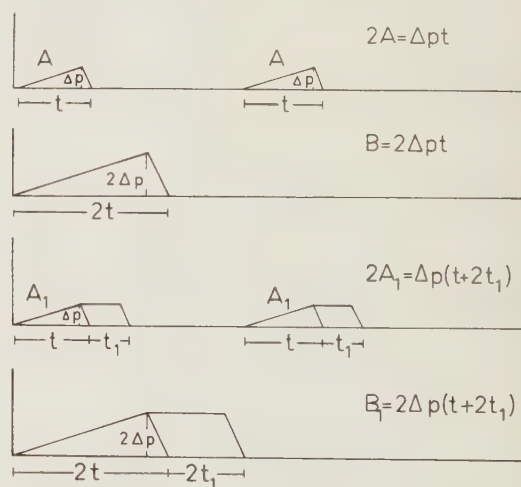


Fig. 25.—Effect of ventilation on intrathoracic pressure increase at different frequencies (2:1). Insufflation flow rate, insufflation time in % of respiratory cycle, and functional residual capacity are constant. See text.

Measurements during dibenoxamine-induced alpha-receptor blockade also showed that the same slight increase in the intrathoracic pressure excites appreciable circulatory changes.

The fact that a low ventilatory frequency combined with an increase of the tidal volume may result in circulatory depression on account of an increased intrathoracic mean pressure seems to have received little attention in current textbooks. The pressure conditions may be illustrated by the principles described by MUSHIN *et al.* (1969). During a given period of time, two breaths A (Fig. 25) are insufflated, each lasting the time t , thus increasing the intrathoracic pressure by the quantity Δp . The average pressure increase during the given period of time may then be represented by the area $\Delta p t$, of the two (approximately) triangular figures. If, at the same flow, twice as large tidal volume, B, is insufflated during the given period of time, the increase in pressure will be twice as large, $2 \Delta p$. (The compliance is presupposed to be the same and linear in both cases). If an EIP with the same proportion of the respiratory cycle is added to the two breaths, the relations will be the same (A_1 and B_1).

The circulatory changes after a change in the ventilatory pattern develop within a few breaths. Blood-gas analyses performed under the same conditions as used in the experiments did not show any changes in P_{aO_2} or P_{aCO_2} within the first few minutes. Blood samples taken immediately before and, on an average, 7 minutes after the change to EIP showed a P_{aO_2} level of 80.7 ± 12.9 mm Hg without EIP and 80.6 ± 15.7 mm Hg with EIP. The P_{aCO_2} was 33.8 ± 2.6 as compared with 32.9 ± 3.0 mm Hg ($n = 11$). The differences are not statistically significant. Thus, the effects on circulation cannot be ascribed to changes in the PO_2 or PCO_2 level of the arterial blood, but must be brought about mechanically. A difference between the values at 20 seconds and 2 minutes after the ventilatory changes could not be found, i. e. a regulatory mechanism which comes into action within this period of time was not observed.

The experiments revealed small or moder-

ate circulatory changes in the presence of normal pulmonary function when low airway pressures were used. It would have been of interest to study the effect of EIP in the presence of impaired function of both the circulatory and respiratory systems. However, attempts to perform experiments in which the circulatory and respiratory function was reduced pharmacologically by histamine, failed on account of the difficulties encountered in obtaining stable experimental conditions, and thus had to be abandoned.

SUMMARY

In experiments on dogs, the circulatory effect of IPPV with and without an end-inspiratory pause (EIP) was studied by continuous measurements of pressures and blood flow in the pulmonary artery or aorta.

A decrease in cardiac output, arterial blood pressure, the stroke work of the right and left ventricles and in the pulmonary conductance could be demonstrated on the addition of an EIP.

On alpha-receptor blockade by dibenoxamine the circulatory effect of EIP became more pronounced. At a slow ventilatory frequency with large tidal volumes the effect on the circulation was further increased.

Simultaneous momentary changes occurred in the stroke volume, the conductance of the pulmonary vessels, as well as in the stroke work of the right ventricle, which may be taken to represent the filling pressure of the right ventricle. An equilibrium between the pulmonary blood flow and the conductance of the pulmonary vessels seems to exist. On the occurrence of rapid variations in the intrathoracic pressure this equilibrium may stabilise the pressure in the pulmonary artery and the arteriovenous pressure gradient.

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